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Vol. 111 **May, 1955** **No. 5**

EDITORIAL

ARTHRITIS

A JOINT is a mechanical masterpiece of nature's design. Its architecture is so superb that the most subtle action can be performed with delicate ease yet it is strong enough to withstand great stress and strain.

The opposed surfaces are co-opted with a liberal precision, and they are buffered and burnished with resilient articular cartilage. The mechanism is controlled and nourished by an intricate arrangement of vessels and nerves and it is lubricated to ensure smooth and flexible action. A healthy joint is more than master of its task; an unhealthy one is inefficient and it can be the seat of pain which may register its effects in distant parts of the body. General systemic disturbances may trace their origin to some lesion of a joint but the reverse is often the case also and general metabolic disorders, and especially those in which pyrexia is a feature, often register their effects in the joints by inflammatory reaction and to the accompaniment of pain and great discomfort.

All animals are subject to inflammatory reactions in their joints and their concomitant effects, i.e., structural changes associated with pain and loss of function. Free and painless movement of the articulations is one of the essential signs of complete good health.

These facts have been known and appreciated from immemorial times and have constantly attracted the attention of those concerned with the healing arts and science.

(*The April issue of The British Veterinary Journal was published on April 28*)

These efforts would seem to have been of little avail. There is a great store of knowledge concerning the normal anatomy and physiology of joints and the morbid macroscopic changes that occur as the result of accident or disease. The histo-pathology of the affected tissues has been under constant study since the microscope enabled us to cast our gaze upon things beyond the purview of the unaided eye and the bacteriologists and the chemists have not been lacking in their zeal to disclose the secrets of nature's deviation from the normal course.

In spite of all this, arthropathy is still a disordered field filled with many conjectural theories and ideas upon which there is no great measure of agreement even on those things which one might assume were matters of fact. Ideas as to the ætiology of the many varieties of arthritis are equally diverse and some of the explanations that have been propounded are of mediocre medieval concept. When the pundits fail to offer either explanation or relief in the case of a disease which is ubiquitous it is not surprising that the clinicians, who have to suffer the constant beseechings of the pain-racked victims, have found a solace and outlet in the mystic abracadabra "Rheumatism," which serves at once as a substitute for all but the most obvious causes of pain in a joint. Mystic words and analgesics may help the practitioner in his dilemma and appease, if only temporarily, the piteous victim, but they are not the worthy product of modern science.

The workers in the field must be stimulated and encouraged to search for the truth. The field is a common one to workers in medical and in veterinary science. Veterinary Surgeons have greater opportunity to follow the experimental approach which can be founded on strictly controlled scientific principles. We would like to see a mass attack made on this crippling disease that brings so much suffering to man and animal. This is one of the diseases in which the fundamental facts are the same whatever the species, and for this reason we welcome the record of Dr. Hughes's experimental investigation on one facet of Arthritis in Pigs. It may be that the humble pig can light the way to the relief of man's intolerable affliction.

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GENERAL ARTICLES

ARTHRITIS IN PIGS. THE EXPERIMENTAL DISEASE INDUCED BY *ERYSIPELOTHRIX RHUSIOPATHIÆ*

By D. L. HUGHES

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THE association of arthritis and swine erysipelas has been recognised for many years and the evidence that this arthritis is a result of infection with *E. rhusiopathiæ* has been shown by a number of workers, including Ward (1922), Craig (1926), Ducksberry (1934), Buitenhuis (1935) and Grey, Osteen and Schoening (1940). Experimental evidence of this association has been provided by Creech (1933), who exposed 22 pigs to infection with *E. rhusiopathiæ*; 5 pigs died and there were 6 non-fatal infections, 5 of which developed arthritis. Ward (1922) had produced arthritis in one pig by the intravenous injection of *E. rhusiopathiæ* and Usdin, Ferguson and Birkeland (1952) were also successful in reproducing arthritis with *E. rhusiopathiæ*.

Arthritis in pigs may be associated with other organisms. Ward (1922) recovered *C. pyogenes* from one case, and pointed out that the arthritis resulting from experimental inoculation with this organism was different in character from that associated with swine erysipelas. Glasser's disease caused by a "serous bacillus" has been confused to some extent with the arthritis caused by *E. rhusiopathiæ*; this is probably an infection with bacteria of the *Hæmophilus* group, as suggested by Shanks (1939) and Sutherland and Simmons (1947), who stressed the inflammation of serous membranes which accompanies arthritis.

Wernery (1937) appears to have been the first author to describe the histopathological changes in the arthritis of swine erysipelas, but there was no detailed account of the process in the joints until Collins and Goldie (1940) published their classic paper on the gross and microscopic pathology of natural and experimentally induced *Erysipelothrix* arthritis. These detailed and comprehensive studies do not appear to have received the attention in veterinary literature which they deserve. Apart from the veterinary interest of their work, attention was drawn to the general resemblance of the condition in pigs to rheumatoid arthritis in man, particularly the gross and microscopic similarities.

It was these similarities which interested us in 1949, because this experimentally induced process might prove suitable for testing the therapeutic value of the adreno-corticoid hormones for their ultimate use in rheumatoid arthritis in man. The condition described herewith was produced in pigs for this purpose but the hopes engendered were not realised. The work is sufficiently interesting in itself to justify description, and not only does it confirm the work of Collins and Goldie (1940) but it serves to draw attention once again to the pathological background of a condition which is common in pigs.

Methods

Pigs. The experimental pigs were Large White Yorkshires born and reared on the premises. Swine erysipelas had not been a problem amongst the pigs which were the source of the experimental animals.

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There were two experiments, in each of which the whole of a litter was used. In Experiment 1 there were 10 pigs, which were injected with *E. rhusiopathiæ* at 17 weeks of age. There were 3 males and 7 females. In Experiment 2 there were 7 pigs, of which 6 were inoculated at 7 weeks of age. There were 5 males and 2 females. The pigs were kept in loose boxes and fed on National Compound pig food. No special conditions of management were used, but as the arthritis progressed it became necessary to lift and help some of the pigs to the trough for feeding.

Inoculation of E. rhusiopathiæ. One strain of *E. rhusiopathiæ* only, E.6, was used in both experiments. This strain was originally isolated from an arthritic hock submitted for examination from a bacon factory. The cultures for inoculation were incubated overnight at 37° C. in serum broth medium. The bacterial counts for these growths varied from 312 to 1,300 x 10^6 organisms per ml.

In Experiment 1 the pigs were inoculated with 5 ml. of culture given intravenously in the ear, half the pigs were injected four times and half were injected twice. Pigs 48, 49, 50, 55 and 56 were inoculated on 27.4.50, 11.5.50, 25.5.50 and 9.6.50, and pigs 51, 52, 54, S and H were inoculated on 27.4.50 and 11.5.50. In Experiment 2 six of the seven pigs were inoculated three times, on 25.5.51, 8.6.51 and 22.6.51. The inoculum was 2 ml. given intravenously to pigs 9, 10, 11, 12, 13 and 15. Pig 14 was not injected but it was retained with the injected pigs.

Clinical observations. No defined scheme of clinical examination was adopted but the pigs were inspected frequently, and in the early stages of the experiment temperatures were taken daily. In Experiment 2 the pigs were weighed at weekly intervals. Blood samples for cultural examinations were withdrawn on many occasions. Certain of the pigs were treated in an attempt to relieve the arthritis but the treatments were without effect. Pig 51 was anæsthetised with sodium pentobarbital to allow a puncture of the knee joint for bacteriological examination. Pig 13 was operated on for prolapsus ani and later was killed because of an irreducible umbilical hernia.

Post-mortem examinations. All pigs were killed by shooting and bleeding, at varying intervals after infection, with the exceptions of pigs 51, H and 10, which died. The internal viscera were examined and then the limbs were severed from the trunk and the joints, including the hips, were dissected. The joints of the vertebral column and the mandibles were not examined as a routine. Bacteriological samples were collected and representative portions of the tissue were taken from the limb joints and the internal viscera for histological examination.

Bacteriological examinations. The following tissues were examined bacteriologically: heart blood, lungs, liver, spleen, kidney, tissues from some of the abnormal joints in the limbs and any of the other structures if showing abnormalities.

Small portions of viscera were removed with sterile precautions, ground in Griffith tubes and sown into 20 per cent cow serum broth and on to the surface

PLATE 1

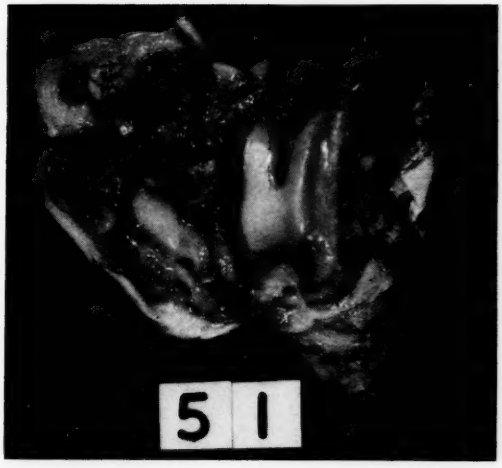

Fig. 1
Pig 51. Stifle. Advanced pannus formation and granulation of synovial membranes.

Fig. 2
Pig 52. Knee. Discoloration of cartilage with some peripheral erosion. Granulation of synovial membranes.

(*Article by Hughes, page* 183)

Fig. 5
Pig 51. Hip. Extensive necrosis of cartilage and synovial membrane resulting from secondary bacterial invasion.

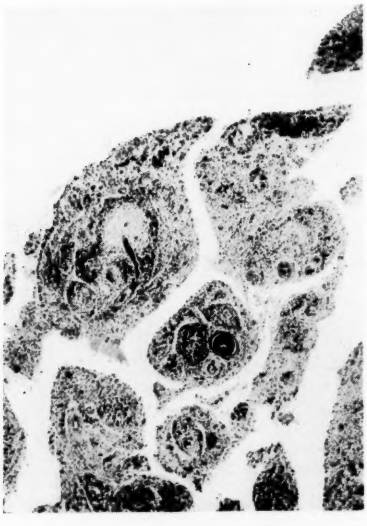

Fig. 6
Pig 13. Hip. Mag. x 75. Inflammatory reaction in synovial villi. Note lymphocyte foci and their relation to blood vessels.

(*Article by Hughes, page* 183)

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PLATE III

Fig. 3
Pig 50. Elbow. Active erosion of cartilage.

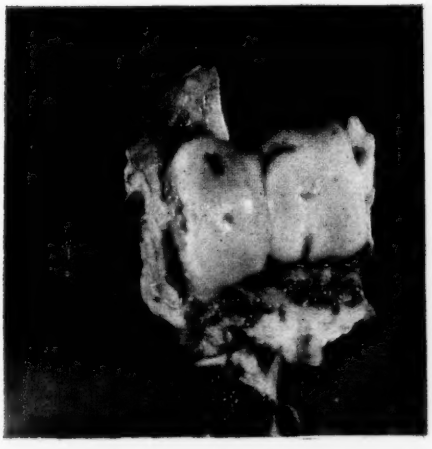

Fig. 4
Pig. 51. Humerus. Various stages of erosion of cartilage. One active ulcer on the left, a healed ulcer in the centre, and fissured cartilage on the bottom edge showing attempt at repair.

(*Article by Hughes, page* 183)

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PLATE V

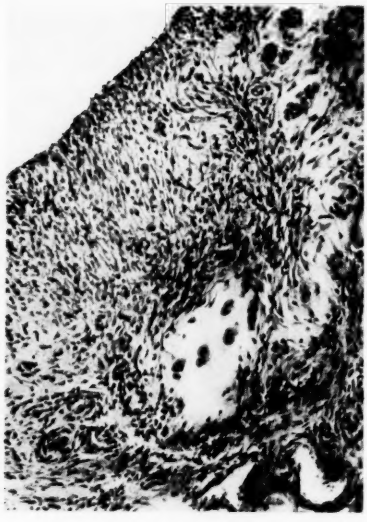

Fig. 11
Pig 15. Stifle. Mag. x 75. Island of normal cartilage in pannus granulation tissue.

Fig. 12
Pig. 10. Elbow. Mag. x 75. Regressive changes in synovial villus. Note relative paucity of inflammatory cells although capillaries are engorged.

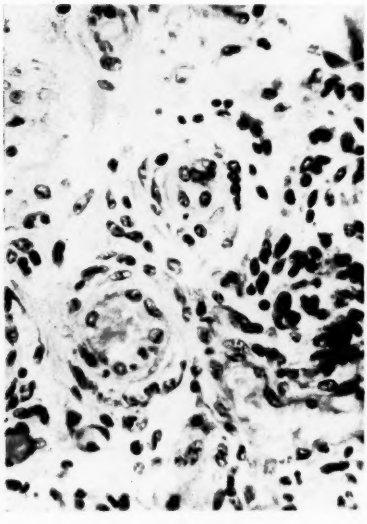

Fig. 13
Pig 12. Stifle. Mag. x 750. Arteritis in synovial membrane. Endothelial swelling, hyaline changes in the media, and peri-vascular infiltration with lymphocytes and plasma cells.

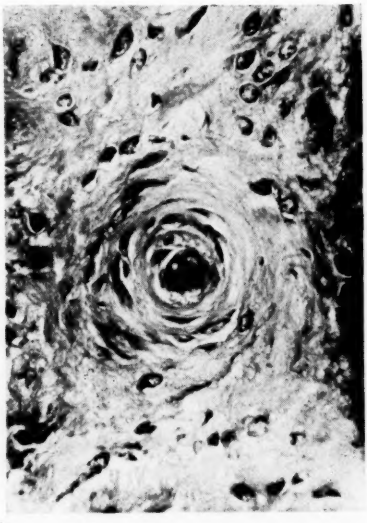

Fig. 14
Pig 12. Stifle. Mag. x 750. Arteritis with obliteration of the lumen.

(*Article by Hughes, page* 183)

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of ox blood agar plates. Heart blood was aspirated from the heart and sown directly into and on to the same media. Joint samples were obtained after careful dissection and opening of the capsule sufficient for the insertion of sterile cotton wool swabs which were rotated within the joint cavity, withdrawn and stroked across the surface of the blood agar plates and then rotated in serum broth medium. The serum broths were incubated for 48 hours at 37° C. and any growth plated on to blood agar. Suspected cultures of *E. rhusiopathiæ* were identified on morphological appearance, biochemical fermentations and characteristic growths in gelatin stab cultures. Occasional strains were tested for pathogenicity in mice.

Histological preparations. Tissues were fixed in Susa's solution or formol saline. Soft tissues were embedded in paraffin; bony material was decalcified with formic acid and doubly embedded in celloidin and paraffin. Sections were stained by hæmatoxylin and eosin, and by Gram's and Giemsa's methods; other stains were also used when considered necessary.

For simplicity in description the joints are referred to by their commonly accepted veterinary names, but for those not familiar with their meaning there follows a list of their anatomical equivalents, the letters in parenthesis referring to the abbreviations used in the tables. Shoulder—Scapulo-humeral joint (F.1). Elbow—Cubital joint (F.2). Knee—Carpal joint (F.3). Fore fetlock—metacarpo-phalangeal joint (F.4). Fore pastern—first fore interphalangeal joint (F.5). Hip—Coxo-femoral joint (H.1). Stifle—Femoro-tibial joint (H.2). Hock—Tarsal joint (H.3). Hind fetlock—metatarso-phalangeal joint (H.4). Hind pastern—1st rear interphalangeal joint (H.5).

Results

None of the pigs developed a clinical condition which could be described as the classic form of swine erysipelas. The temperature reactions were trivial, on a few occasions one or two pigs exhibited temperatures of 104° to 104.4° F., but these were exceptional. Before the course of inoculations with *E. rhusiopathiæ* were completed a number of pigs showed slight swelling of some of their joints and three showed a transient erythema of the abdominal skin. Within a fortnight of the last injection in Experiment 2, all 6 injected pigs were lame. However, the lameness which developed varied in intensity from week to week and appeared to arise from different joints on different occasions. As the condition progressed the process tended to localise in a particular joint or joints and the lameness was associated with those joints, but this took many weeks to occur. Eventually, in some pigs, the injury to joints resulted in almost continuous recumbency, and certain animals would have failed to eat unless lifted to the trough. Nevertheless, most of the pigs made steady weight gains. A number of the animals, especially in Experiment 1, in which they were kept for longer, showed a form of hyperkeratosis, especially of the lower limbs. This was thought to be due to a chronic irritation caused by micturition whilst recumbent, but later these skin lesions were observed on the back and shoulders of some pigs. The cause of this hyperkeratosis was not determined.

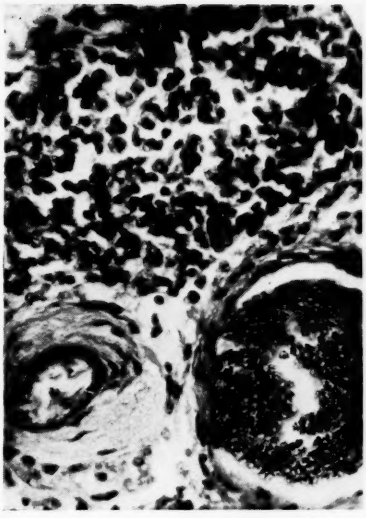

Fig. 7
Pig 13. Hip. Mag. x 750. Lymphocyte focus in synovial villus, consisting of lymphocytes and plasma cells.

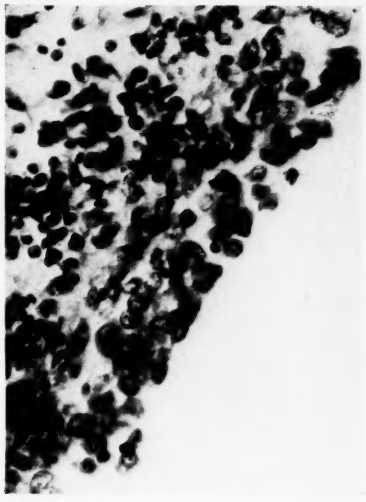

Fig. 8
Pig 13 Hock. Mag. x 750. Proliferation of intimal cells of a synovial villus.

Fig. 9
Pig 11. Head of tibia. Mag. x 75. Pannus formation overlying articular cartilage.

Fig. 10
Pig 11. Head of tibia. Mag. x 75. Ulceration of cartilage. Note connection between granulation tissue in ulcer and pannus overlying cartilage.

(*Article by Hughes, page* 183)

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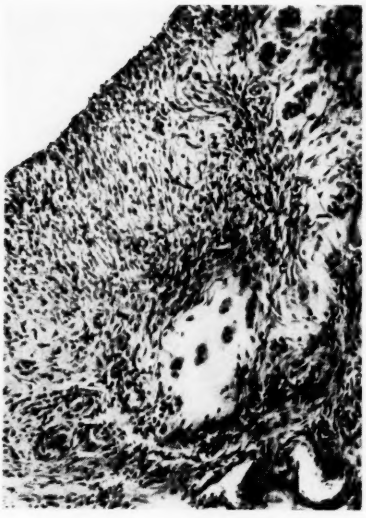
PLATE V



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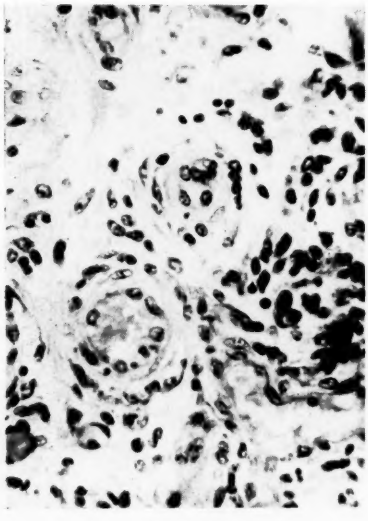

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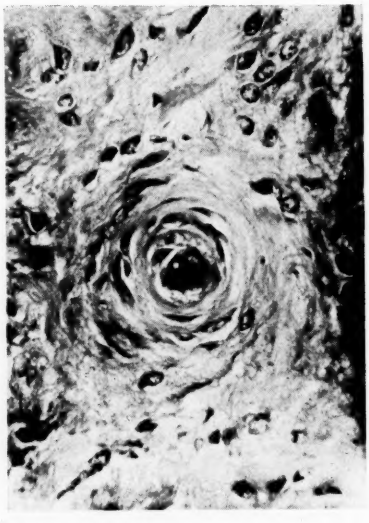

Fig. 14
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(*Article by Hughes, page* 183)

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TABLE X

A SUMMARY OF PATHOLOGICAL AND BACTERIOLOGICAL FINDINGS.

Pig No.	Weeks since Infection	Viscera: Heart P	Heart B	Lungs P	Lungs B	Liver P	Liver B	Spleen P	Spleen B	Kidney P	Kidney B	Lymph Glands P	Lymph Glands B	Fore Limb Joints: F.1 P	F.1 B	F.2 P	F.2 B	F.3 P	F.3 B	F.4 P	F.4 B	F.5 P	F.5 B	Hind Limb Joints: H.1 P	H.1 B	H.2 P	H.2 B	H.3. P	H.3. B	H.4 P	H.4 B	H.5 P	H.5 B	No. of Joints with gross change / No. of Joints examined	Erysip. positive / No. of Joints examined	Comments
49	13	0	e	0	0	0	0	0	0	0	0	Rt. Iliac ++	e	R 0	/	0	/	0	0	0	/	0	/	±	/	+++	e	+++	/	++	/	/	/	3/19	1/3	
														L ±	/	0	/	0	0	0	/	0	/	±	/	0	/	0	/	0	/	0	/			
48	22	0	0	0	β	0	0	0	0	+	/	0	/	R ±	0	±	/	0	/	0	/	0	/	+	0	+	/	++	/	++	/	0	/	6/19	1/4	
														L ±	/	++	/	++	/	●	/	/	/	++	/	±	/	+++	e	±	0	±	/			
52	35	0	0	0	0	0	0	0	0	0	0	Lt. Popl. +	0	R ±	0	++	0	+++	0	±	/	/	/	0	0	±	e	+	/	±	/	/	/	6/16	3/9	
														L ++	0	++	/	±	/	0	/	/	/	0	0	+++	e	++	e	0	/	/	/			
91	52	++	β	0	/	0	β	0	β	+	β	Inf.Cerv. +	e	R +++	β	+++	β e	±	/	0	/	0	/	+++	β	+	/	++	β e	+++	/	+++	/	11/20	4/8	Mild Pleuritis. β Streptococcus secondary invader.
														L +++	β	0	/	+++	β e	++	/	0	/	+++	β e	+++	β	+	/	0	/	0	/			
93	62	±	β	0	/	0	βe	0	e	0	0	Iliac ++	0	R 0	/	0	/	0	/	0	/	0	/	+++	e	+++	β	±	/	0	/	+	e	5/20	1/7	Secondary invasion Pasteurella, Staph.pyog. C. pyogenes.
														L ±	0	++	0	+++	e	±	/	0	0	+++	/	0	/	0	/	0	/	+	/			
50	67	+	0	0	e	0	0	+	0	+	0	Rt. 0	0	R ±	/	±	0	0	/	0	/	0	/	0	/	+++	e	+++	0	/	/	0	/	5/19	5/7	
														L 0	/	+++	e	0	/	0	/	0	/	+++	e	+++	e	±	e	0	/	0	/			
8	80	0	0	0	0	0	β	0	0	±	β	Iliac +	e	R 0	/	±	0	±	0	0	/	0	/	0	/	+++	e	0	/	+	/	+	/	3/20	3/6	β Streptococcus in Liver and Kidney
														L ±	/	0	/	+++	e	0	/	0	/	+++	/	+	0	+	e	0	/	+	/			
11	83	/	β	Considerable post mortem change		/	/	/	/	/	0	+	0	R +++	e	+	/	0	/	++	β	+	/	0	/	+++	β e	+++	e	+	/	+	β	8/20	6/8	Died. β Streptococcus secondary invasion.
														L 0	/	+	/	++	β e	+	/	±	/	+++	/	±	e	+++	β e	++	/	0	/			
54	86	0	0	0	/	0	0	0	0	0	0	0	/	R +	/	0	/	0	/	±	/	0	/	+++	/	+	/	+	/	±	0	0	/	4/20	0/6	Signs of regression
														L ++	0	++	0	+	/	0	0	0	/	+++	/	0	/	+	0	±	0	0	0			
56	90	0	0	0	/	0	0	0	0	0	0	0	/	R ++	0	++	0	++	0	+	0	0	/	+	/	++	/	0	/	+	0	0	/	8/20	0/9	β Streptococcus in 1 joint. Signs of regression.
														L +	0	++	0	++	β	++	/	0	/	++	/	0	/	±	/	±	0	0	/			
12	18	0	0	0	0	0	0	0	0	0	0	Illiac +++	e	R 0	/	++	e	+	/	0	/	0	/	0	0	+++	e	+++	e	++	e	b	b	5/20	6/12	
														L 0	/	±	0	+	e	0	/	0	/	0	0	0	/	+++	e	0	0	0	b			
13	22	0	0	0	0	0	0	0	0	0	0	0	e	R 0	/	++	e	±	/	0	/	0	/	+++	e	0	/	++	e	0	/	0	/	5/20	4/6	Herniae
														L 0	/	++	0	0	/	+	0	±	/	0	/	+	/	++	e	0	/	0	/			
9	35	+	0	0	/	±	0	±	0	0	0	0	/	R 0	/	+++	β e	+++	/	±	/	±	/	0	/	0	/	+++	β e	0	/	0	/	6/20	5/6	Streptococcal and Staphylococcal as secondary invaders
														L 0	/	+++	β es	0	/	0	0	0	/	++	e	0	/	+++	e	0	/	0	/			
11	39	±	0	0	/	0	0	0	0	++	0	0	/	R 0	/	++	/	+++	0	0	/	0	/	/	/	+++	e	/	/	/	/	/	/	5/16	3/4	
														L 0	/	+++	e	±	/	0	/	0	/	0	/	+++	e	+	/	0	/	0	/			
10	39½	/	0	Post mortem change		/	/	/	0	/	0	++	0	R 0	/	+++	e	+++	0	0	/	0	/	++	e	+++	e	++	0	0	/	0	/	9/20	4/7	Died
														L 0	/	++	/	+++	β	++	/	0	/	++	e	0	/	±	/	±	/	±	/			
15	42	0	0	/	/	0	0	0	0	+	0	0	/	R 0	/	0	/	0	/	0	/	0	/	+++	e	+++	e	+++	/	0	/	0	0	8/19	6/8	
														L /	/	++	e	++	0	+	/	0	/	+++	e	++	e	+++	e	0	/	0	/			
TOTALS		Path. No. with gross changes / No. examined						Bact. No. Erysip. positive / No. cultured						6/31	1/10	19/32	9/18	13/32	5/15	4/32	0/5	0/29	0/1	17/31	8/15	15/32	14/17	17/31	14/17	5/30	1/6	1/28	0/6	97/308	52/110	

P. = pathological findings in joints.
+++ = erosions, pannus, granulation
++ = granulation, early pannus
+ = congestion
± = slight congestion
0 = apparently normal
/ = not examined

Fore Limb Joints: F.1 = shoulder; F.2 = elbow; F.3 = knee; F.4 = fetlock; F.5 = pastern. R = right leg.

Hind Limb Joints: H.1 = hip; H.2 = stifle; H.3 = hock; H.4 = fetlock; H.5 = pastern. L = left leg.

B. = bacteriological findings
e = Erysipelothrix positive
β = haemolytic streptococcus positive
c = C. pyogenes positive
p = Past. septica "
s = Staph. pyogenes "
0 = negative
/ = not cultured

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In Experiment 2 blood samples for bacteriological culture were withdrawn on 61 occasions from different pigs while alive, including the uninjected Pig 14. *E. rhusiopathiæ* was recovered once only from such samples; this was from Pig 13, 10 days after its first injection of *E. rhusiopathiæ*. A number of urine and fæces samples were also examined, but with negative results.

Pathological Changes

The account which follows is a summarised description of the various features of the disease seen in all of the 16 animals. The bacteriological and pathological findings are tabulated in Table I and a detailed account of two typical post-mortem examinations are given in the appendix.

The morbid changes in the joints were essentially a replacement of the synovial membranes by excessive granulation tissue which extended as a pannus formation on to the articular surfaces of the cartilage, and erosion of the articular cartilages which was followed by adhesions and ossification.

The granulation began as a congestion of capillaries in the synovial membrane and this was followed by proliferation of synovial villi. In some joints this proliferation progressed until the membranes were a rugose velvety mass (Fig. 1, Pig 51, Stifle), the gross appearance of which resembled red turkish towelling. Some of the enlarged villi were fingerlike and in some of these the tips were flesh coloured, being separated from the congested remainder of the villus by a plum coloured line of demarcation. The articular cartilages varied in colour from a deep dusky red (Fig. 2, Pig 52, Knee), to a purplish grey or even dead white, according to the activity of the process in the joint.

Pannus formation was a frequent feature in affected joints. Its extent varied from a well-marked reduction of the articular area due to even advance of the pannus from the edge of the articular surfaces (Fig. 1, Pig 51, Stifle), to small wedge-shaped areas, the bases of which lay at the margin of the cartilage. In some joints the erosions were extensive, involving a considerable proportion of the bearing surface of the cartilage (Fig. 3, Pig 50, Elbow). In others, erosion was shown as nail head sized ulcers with red granulating bases penetrating deeply into the articular cartilage (Fig. 4, Pig 51, Humerus). On the other hand a joint might show extensive and gross change of the synovial membrane without ulceration of the articular cartilage. One formed the impression from some of the long standing cases (see Pig 54) that cartilage had considerable powers of low grade repair. This was shown by healed erosions with some distortion of articular cartilage and lacking the pearly lustre of normal cartilage (Fig. 4, Pig 51, Humerus). In some areas there was crinkling and fissuring of the cartilage and occasionally there was a layer of false cartilage lying over normal articular cartilage. Fibrous adhesions had formed between some opposing ulcerous surfaces, and in long standing cases these adhesions had ossified, resulting in ankylosis of the joint. In one or two joints this ankylosis was so advanced that dissection of the joint was impossible.

In pigs 51, 55 and H, the joints presented lesions which were not typical of uncomplicated *E. rhusiopathiæ* infection; these were long standing cases in

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which secondary bacterial invasion had occurred. In some of these joints there was necrotic destruction of the articular cartilages to such an extent that little normal cartilage was left (Fig. 5, Pig 51, Hip). This destructive process also affected the synovial membranes, which showed pockets of necrosis and even fistulæ into the adjacent musculature. Some of these joints showed well-marked periarticular fibrosis, and in others the joint capsules were distended with a turbid joint fluid. Excess joint fluid was not a feature of uncomplicated arthritis due to *E. rhusiopathiæ*.

Gross pathological changes in other organs were not a conspicuous feature of the infection, although some lesions were seen in certain pigs.

None of the pigs exhibited the characteristic endocardial vegetations which are described in certain forms of the natural disease. Pig 51 was suffering from a uniformly distributed fibrinous pericarditis which made dissection of the pericardium from the epicardium difficult. Cultures from the pericardial surface were contaminated, but a β hæmolytic streptococcus was isolated from the heart blood and other visceral organs. Pigs 55 and 11 showed restricted areas of vascular disturbance on the endocardial surface of the left ventricle. In Pig 55 this occurred as a fine network of capillary engorgement on the papillary muscles of the chordæ tendinæ and in Pig 11 as petechial hæmorrhages under the mitral valves. In Pigs 50 and 9 the hearts were dilated, pale and flabby with a slight thickening of the edges of the mitral valve in Pig 9.

Six pigs presented macroscopic lesions in their kidneys:—a pale lesion 2 to 3 cm. in length in the cortex of the left kidney in Pig 48, pyelonephritis in Pigs 51 and H, and a β hæmolytic streptococcus was recovered from that in Pig 51, Pigs 50, 11 and 10 showed some congestion of the medullæ, the cortices were pale with white or reddish striations, and in Pig 11 there were also pin point white foci in the cortex. Changes in other organs were limited to varying degrees of cloudy swelling and congestion. Lymph glands draining limbs with obvious arthritic changes were sometimes swollen, the increase in size was marked, the cut surfaces were a mottled red and some were cystic. Wernery (1937) has drawn attention to the value of examining associated lymph glands for determining which limbs should receive further attention in meat inspection.

Histopathology

In the acutely inflamed joint there was a lymphocyte and plasma cell infiltration in the synovial villi (Fig. 6, Pig 13, Hip); these lymphocytes and plasma cells tended to aggregate in typical foci (Fig. 7, Pig 13, Hip). There was a proliferation of the synovial intima several layers of cells in thickness (Fig. 8, Pig 13, Hock). The pannus formation was an extension of the inflammatory process in the synovial membranes and it was closely adherent to the underlying articular cartilage, except at its free edge (Fig. 9, Pig 11, Head of Tibia). There was some invasion and destruction of articular cartilage by the overlying pannus and in some joints there was an accompanying inflammatory reaction in the marrow under the cartilage. In many sections it was clear that ulceration of cartilage was a direct extension of the inflammatory changes

in synovial membranes and pannus (Fig. 10, Pig 11, Head of Tibia). In some lesions the destruction of the articular cartilage extended into the sub-chondral bone and the breach was filled with granulation tissue. The granulation tissue sometimes contained isolated fragments of apparently normal cartilage (Fig. 11, Pig 15, Stifle, Femur).

In certain joints active inflammatory changes had regressed, the picture in the synovial villi was less cellular in nature and lymphocyte foci were infrequent. Although the villi were enlarged, inflammatory cells were few, but capillary engorgement was still present (Fig. 12, Pig 10, Elbow).

In acute swine erysipelas endothelial damage is a characteristic feature and in this chronic infection damage to small vessels was also seen. This took the form of an arteritis shown by endothelial swelling and hyaline changes in the media, usually accompanied by some peri-vascular infiltration with lymphocytes and plasma cells (Fig. 13, Pig 12, Stifle). Occasionally the endothelial swelling had advanced to the stage of obliterating the lumen of the vessels (Fig. 14, Pig 12, Stifle).

Bacteriological Results

The outstanding bacteriological feature of the disease was the persistence of infection in the joints. In only two pigs, 54 and 56, were there failures to recover *E. rhusiopathiæ*. These two pigs had survived for 86 and 90 weeks after infection respectively and in both animals there was some pathological evidence of regression of the disease. On the other hand Pig H, which died 83 weeks after infection, yielded *E. rhusiopathiæ* from six of eight joints examined. Although most of the pigs were carrying *E. rhusiopathiæ* in their joints, a considerable number of joints showing pathological change were apparently negative. These negative results may be a reflection of the limitations of bacteriological technique, for in some cases the number of *E. rhusiopathiæ* isolated was small.

E. rhusiopathiæ was not recovered from the internal viscera of the pigs with the exception of a positive heart blood culture from Pig 49, who was killed 13 weeks after infection. In this connection the positive blood culture obtained from the live pig, 13, ten days after the first injection of culture should be remembered.

E. rhusiopathiæ was isolated from a number of lymphatic glands; these were draining affected legs and in all instances, except Pig 13, showed marked lymphadenitis.

Pigs 51, 55, S, H, 56 and 9 were all examples of secondary invasion with other bacteria; these were β hæmolytic streptococci, *C. pyogenes* and *Pasteurella septica*. In four animals the strains of streptococci isolated could not be assigned to Lancefield's serological groups but those recovered from pigs 56 and 9 belonged to Group C.

The sera from dead pigs 11, 10 and 15 agglutinated *E. rhusiopathiæ* to dilutions of 1/2560 in Pigs 11 and 10, and a trace in a dilution of 1/1280 in Pig 15. Pig 14, the uninjected pig, was killed after 28 weeks of pen contact with the six infected pigs in Experiment 2. No gross changes were observed

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in its joints apart from slight synovial congestion in some of the distal ones in the hind legs. *E. rhusiopathiæ* was not recovered from the four joints cultured and the serum showed only a trace of agglutination at a dilution of 1/20.

Discussion

It is clear that repeated injections of *E. rhusiopathiæ* in pigs can give rise to a chronic proliferative arthritis. Ward (1922) and Collins and Goldie (1940) had already demonstrated this and they described the changes in the joints and in those occurring in the natural disease. The description given by Wernery (1937) of the arthritis seen in the course of meat inspection from which *E. rhusiopathiæ* could be recovered also emphasises that the naturally occurring arthritis is the same as the experimentally induced disease.

It is curious that despite this evidence L. P. Doyle (1951) in the U.S.A. found it difficult to accept *E. rhusiopathiæ* as the casual agent of this form of arthritis and he stated that " It is perhaps correct to say that the cause is not known." Doyle quoted the facts that *E. rhusiopathiæ* cannot always be recovered from affected joints, and that swine erysipelas cannot always be caused in pigs with cultures of *E. rhusiopathiæ,* and doubted the ætiological role of this organism. From our results, and others, it can be seen that only a proportion of joints typically affected in the experimental pigs yielded *E. rhusiopathiæ* on culture. Nevertheless, the affected negative-joints differed in no pathological way from bacteriologically-positive-joints.

Furthermore, in the course of examining many natural arthritis joints submitted from a bacon factory, we have seen a number with typical erysipelas changes; some of these yielded *E. rhusiopathiæ,* others did not.

Insofar as the difficulty of reproducing the disease is concerned it should be pointed out that all 16 pigs in our series developed the typical arthritis after repeated intravenous injections of *E. rhusiopathiæ*. Collins and Goldie (1940) were also successful in all 8 pigs similarly injected. Usdin, Ferguson and Birkeland (1952) were able to reproduce this arthritis in 7 out of 8 pigs injected with culture; the exception died early in the observations. T. M. Doyle (1947) has demonstrated that with appropriate techniques the acute form of swine erysipelas can also be induced by injections of *E. rhusiopathiæ*.

Finally, the ability of *E. rhusiopathiæ* to produce changes in joints is not limited to pigs, it has been described in horses, Paterson and Heatley (1938), lambs, Stamp and Watt (1947), Murnane (1938); rabbits, Goldie and Collins (1951); and calves, Moulton, Rhode and Wheat (1953). The last authors published photo-micrographs showing changes similar to those in pigs.

There does not seem to be any doubt of the ætiological role of *E. rhusiopathiæ* in chronic proliferative arthritis in swine. This does not mean that other organisms cannot give rise to arthritis in pigs, but the arthrites so caused are different in character. It must also be remembered that a primary joint infection with *E. rhusiopathiæ* may become complicated with secondary invading bacteria. There were six such pigs in our experiments. The arthritis which arises naturally may be the sequel to an observable attack of acute swine

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erysipelas, although many pigs appear to develop arthritis without any previous symptoms of erysipelas It is reasonable to assume that in either case the arthritis arises as a result of a bacteræmia. In our experimental pigs there was one positive blood culture at post-mortem in Pig 49, 13 weeks after infection, as well as the recovery of *E. rhusiopathiæ* from the blood of the live Pig 13, ten days after its first injection. In the course of routine post-mortem diagnosis a pig was examined which had acute erysipelas; *E. rhusiopathiæ* was recovered from heart blood, internal viscera and from all the twelve joints cultured. In this animal arthritic changes had not had time to develop.

Although *E. rhusiopathiæ* reaches the joints via the blood-stream we do not know whether the changes in the joints are a direct result of the presence of the organisms. Collins (1949), in discussing the ætiology of human rheumatoid arthritis, suggests that the joint changes in that disease may result from repeated hæmatogenous bacterial infection of the joints and a resulting sensitisation of joint tissues. A sensitisation of this sort would explain the grossly inflamed joints from which *E. rhusiopathiæ* cannot be isolated. In setting up experimental arthritis in pigs more than one injection seems to be necessary and this lends support to the suggestion of sensitisation. However, even if arthritis is incurred after one injection only, the joints may receive repeated doses from some other focus in the body set up by the injection.

In view of the persistence of *E. rhusiopathiæ* in some arthritic joints, pigs with arthritis must be regarded as possible sources of infection. How dangerous such sources of infection may be is not clear. Collins and Goldie (1940) had two pigs develop arthritis after pen contact with experimental arthritic pigs. Craig (1926) has also presented evidence that infection can spread from arthritic pigs. On the other hand, our Pig 14, the uninjected "control," presented no evidence of infection with *E. rhusiopathiæ* after 28 weeks of close contact with the infected pigs in Experiment 2.

Summary

An arthritis was induced experimentally in all sixteen pigs given repeated intravenous injections of cultures of *Erysipelothrix rhusiopathiæ*. These inoculations of organisms failed to cause systemic signs of erysipelas other than arthritis. Blood cultures soon became negative and in the live pig were not positive later than 10 days after the last inoculation. On post-mortem examination *E. rhusiopathiæ* was only recovered from one heart blood culture, in the first pig to be killed, 13 weeks after the last inoculation. However, affected joints yielded positive cultures up to 83 weeks after the last injection.

The arthritis was multiple (from 3 to 11 joints in each animal). Out of the total of 308 joints examined, 97 showed gross changes, and 52 of the 110 joints examined bacteriologically were positive for *E. rhusiopathiæ*.

The joints most frequently affected were elbow, hip, hock, stifle and knee in this order. Visceral changes were trivial and scanty, although lymphatic glands regional to affected limbs often showed lymphadenitis and cultures from them were sometimes positive.

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The relationship of this experimental arthritis to the arthritis occurring naturally in association with swine erysipelas is discussed.

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APPENDIX

Detailed post-mortem records of two pigs

Pig 50 ♀

EXPERIMENT 1.—Infected by four intravenous injections of *E. rhusiopathiæ* on 27.4.50, 11.5.50, 25.5.50 and 9.6.50. Killed by shooting and bleeding on 25.9.51, 67 weeks after injection. The pig had been treated with chloramphenicol from 3.9.51 to 7.9.51 without any effect.

POST-MORTEM EXAMINATION:

When killed it was underweight for its age and size. There was hyperkeratosis, especially on the hind limbs and the back.

Heart. Pale and flabby, the outer portion of the myocardium of the right ventricle was irregularly white in colour. No valvular lesions. (Bact. neg.)

Lungs. Innumerable petechial hæmorrhages in both lungs, abundant frothy fluid in trachæ and bronchi. ? agonal effects. (*C. pyogenes* +).

Spleen. Enlarged and fibrous. (Bact. neg.)

Liver. Friable. „ „

Ovaries. Cystic. „ „

Kidneys. Capillary congestion. „ „

Iliac Lymphatic Nodes. Enlarged, fibrous and contained cystic loculi. (Bact. neg.).

Ileo-Cæcal Valve. A dozen small ulcers containing caseous material which shelled out easily.

LIMBS.

Right Fore Leg

Shoulder: Slight patchy congestion of synovial membrane. Elbow: Slight patchy congestion of synovial membrane (*E. rhusiopathiæ* not recovered). Knee: Only one row of articulations examined which were normal. Fetlock: Normal. Pastern: Normal.

One external aspect of the elbow was a large encapsulated abscess containing half-pint of greenish creamy pus. (*C. pyogenes* +.)

Left Fore Leg

Shoulder: Normal. Elbow: Pink-coloured joint fluid causing some distention of the joint capsule. Abundant granulation tissue of synovial membranes and dark red ulcerations on both articular surfaces. Process very active. (*E. rhusiopathiæ* +.) Knee: Normal. Fetlock: Normal. Pastern: Normal.

Right Hind Leg

Hip: Normal. Stifle: Considerable periarticular thickening and a very fibrous joint capsule. Extensive raspberry jam-like granulation of synovial membrane. Distortion and thickening of articular surface of internal condyle of femur, with pannus formation. Ulcerous pitting of articular surfaces of tibia. (*E. rhusiopathiæ* +.) Hock: Pinkish-coloured granulation tissue of synovial membrane, with erosion on bearing surfaces of astragalus and tibia. Lower row not dissected. (*E. rhusiopathiæ* not recovered.) Fetlock: Not opened. Pastern: Normal.

Left Hind Leg

Hip: Extensive and exuberant dark red granulations of synovial membranes, in some areas like bunches of grapes. Early pitting of articular surfaces with advancing ulceration from edges of articular head of femur. (*E. rhusiopathiæ* +.) Stifle: Considerable granulation of synovial membrane and fibrosis of joint capsule. Pannus and pitting of articular surface of external condyle of femur. (*E. rhusiopathiæ* +.) Hock: A healed erosion on articular surface of tibia. (*E. rhusiopathiæ* +.) Fetlock: Normal. Pastern: Normal.

Pig 15

Experiment 2.—Infected by three intravenous injections of *E. rhusiopathiæ* on 25.5.51, 8.6.51 and 22.6.51. Lame on both hind legs and possibly on the left fore leg. Degree of pain was not marked. Killed by shooting and bleeding 16.4.52, 42 weeks after last injection.

Post-mortem Examination:

Poor bodily condition. Slight hyperkeratosis of the limbs. Heart: Contracted and empty. Valves normal. (Bact. neg.). Liver: Friable with some autolysis. (Bact. neg.). Spleen: Normal. (Bact. neg.). Kidney: Numerous indistinct foci in the cortices, which were not clearly demarcated from medullæ. (Bact. neg.). Stomach: Empty with some bile staining. Ileo-cæcal valves: Usual amount of inspissated material in the crypts.

Limbs.

Right Fore Leg

All joints were normal.

Left Fore Leg

Shoulder: Not examined. Elbow: Granulation tissue of synovial membrane. Active small erosions on the head of radius. (*E. rhusiopathiæ* +.) Knee: Pronounced granulation of synovial membrane but no erosions of carti-

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lage. (*E. rhusiopathiæ* neg.) Fetlock: Granulation tissue in the internal half of the joint. Pastern: Normal.

Right Hind Leg

Hip: Considerable granulation of synovial membrane. Some erosion of cartilage on femoral head advancing from its periphery. (*E. rhusiopathiæ* +.) Stifle: Distended with turbid fluid. Gross granulation tissue formation. Pannus on femoral surface. Granulation tissue on semilunar cartilages. (*E. rhusiopathiæ* +.) Hock: A pouching bursa containing fluid and granulation tissue, the villi had white necrotic tips. Also typical granulation tissue around upper articulation. Lower row normal. No erosions. Fetlock: Normal. Pastern: Normal. (*E. rhusiopathiæ* neg.)

Left Hind Leg

Hip: Granulation tissue with some erosion of femoral cartilage from periphery. (*E. rhusiopathiæ* +.) Stifle: Œdematous granulation with early pannus formation of femur. (*E. rhusiopathiæ* +.) Hock: A congested pouching bursa, size of bean, on anterior surface, filled with granulation tissue. This was continuous with exuberant granulation of synovial membrane in top row of joint. (*E. rhusiopathiæ* +.) Fetlock: Normal. Pastern: Normal.

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OBSERVATIONS ON SOME PRELIMINARY DOSING TRIALS WITH PHENOTHIAZINE ON HILL LAMBS IN SOUTHERN SCOTLAND

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with

A Statistical Appendix
By E. C. R. REEVE

Introduction

YOUNG sheep suffer more severely from helminthiasis than older sheep and in early July on hill farms in South East Scotland and in the basin of the Border Esk about 28 per cent and 54 per cent respectively of the lambs, when still under three months old, have worm egg counts of at least 500 eggs per gram. of fæces; nearly a third and a half respectively of these percentages are counts of not less than 1,000 e.p.g. (Parnell, Rayski, Dunn and Mackintosh, 1954*b*). After a slight decrease in the levels at the end of July, the percentages of heavily infested lambs increase again to higher numbers within the next two months. In other districts of Scotland a lower, but still considerable, proportion of hill lambs carry seriously heavy infestations (Parnell, *et al.*, 1954*a*).

In Southern Scotland the rapid increase in the worm egg counts of lambs in late June and early July is caused chiefly by *Ostertagia* spp. and by *Nematodirus* spp., and after the slight fall in output, which starts in the middle of July and lasts for a few weeks, the increase which follows is caused principally by *Trichostrongylus* spp.; *Bunostomum trigonocephalum* augments it, and occasionally *Hæmonchus contortus* increases it further (Morgan, Parnell and Rayski, 1950, 1951, 1952; Parnell, *et al.*, 1954*a* and *b;* and Parnell, 1954).

The serious loss of meat caused by worms in lambs has been emphasised by Taylor (1953), who has stated that " experiments with twin lambs have shown that a very ordinary infestation of stomach worms is sufficient to cause a loss of 20 or 30 lb. mutton per head "; with Scottish Blackface and Cheviot lambs, and those of other hill breeds, the loss is undoubtedly less, as Taylor's observations were on larger sheep. Nevertheless, since there are about two million lambs on Scottish hills in summer, and almost as many on the hills of England and Wales, the total loss of meat in the United Kingdom is considerable and its reduction is an urgent problem.

During 1951 and 1952 preliminary anthelmintic dosing trials were made on hill lambs to determine the effects of summer dosing on worm egg production and on the weight gains of the lambs. Phenothiazine alone was tested, and the trials were confined to farms in Southern Scotland: the results would not necessarily apply to farms near the West Coast, where infestations of *Ostertagia* spp. in lambs during July are lighter than in other districts of Scotland (Parnell, *et al.*, 1954*b*, and Wilson, *et al.*, 1953).

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Materials and Methods

The results were judged by worm egg counts and body weights; an increase in weight is the primary reason for dosing lambs.

During 1951 and 1952, the trials with phenothiazine were made on hill lambs on farms in South East Scotland and in the basin of the Border Esk. A single heavy dose (17 to 20 gm.) of phenothiazine as a suspension was given between late June and early August, when it might be expected to be most effective. Most of the trials were on commercial farms, through the generous co-operation of the farmers. Individual identification with ear tags was practicable on one farm only (B), where trials were carried out in both years.

The control lambs received the same amount of handling as the dosed lambs.

In 1951 trials were carried out on a farm (A) near the west end of the Lammermuir Hills and on a farm (B) on the north east end of the Cheviot Hills.

In 1952 lambs were dosed early in July on farm B, in the middle of July on a farm (C) on the western end of the Cheviot Hills, and early in August on two farms (D and E) further west near the River Esk. All these farms are typical of this part of Scotland, with very little heather.

On farm A the lambs were Scottish Blackfaces; on the other farms they were Cheviots, except on farm C, where they were first crosses of these two breeds; the helminth infestations of Blackfaces and Cheviots are, however, comparable (Morgan, *et al.*, 1950).

On each of these farms the ewe lambs of one or more hefts, depending on the size, were divided into two equal groups; a coin was spun to decide which half should be dosed and which half should be the controls.

At the time of dosing and a month or six weeks later the lambs were weighed and fæces samples were collected. Worm egg counts were made by the modified McMaster technique (Morgan, *et al.*, 1950). The eggs of *Strongyloides* spp., of *Nematodirus* spp. and of the "Other Strongyles"* were counted separately. Phenothiazine is reputed not to be very efficacious against *Strongyloides papillosus* and *Nematodirus* spp., but to be fairly effective against the adults of most of the Other Strongyles, if fairly heavy doses are given.

Cultures were made from the lamb fæces at the end of the trials, and the larvæ from them extracted, identified and counted.

Results

The statistical analyses are given in the appendix, and a few points are noted here. Worm egg counts tend to be very skew in their frequency distribution, and a modified logarithmic transformation has been used, and the estimates of the effects of dosing, quoted in Table I, were obtained from the analysis of the transformed counts. The effects on the final comparisons of differences between the worm egg counts of the dosed and of the control groups at the time of dosing were also tested; it appears that initial differences in the means of the worm egg

* "Other Strongyles," or "O.S.," include all the Strongyle eggs found in these sheep, with the exception of *Nematodirus* spp.—"N."

counts are not likely to be reflected in the final counts, so that the differences in the means of the worm egg counts at the end of the trials can be taken as direct measures of the effect of dosing. Some carry-over effect must be expected, however, in body-weights, and for every pound of difference at the start of the trial the difference at the end of the trial should be, on an average, 1.3 lb.; this factor has been used in eliminating the effect of initial weight differences between the dosed and control means from the final comparisons shown in Table III.

Table I.

Mean numbers of eggs of Other Strongyles and of Nematodirus spp. per gm. of faeces at the beginning and end of each trial, and the effect of dosing measured as the percentage difference in the dosed compared with the control lambs at the end of the trials.

Farm.	Start of trials: Date.	Start of trials: Mean of all lambs. O.S.	Start of trials: Mean of all lambs. N.	End of trials: Date	End of trials: Mean of control lambs. O.S.	End of trials: Mean of control lambs. N.	Effect of Dosing, (1). Dosed-control mean count as percentage of control mean for final counts. O.S.	Effect of Dosing, (1). Dosed-control mean count as percentage of control mean for final counts. N.
A.	30 Jun. '51.	675.	235.	4 Aug. '51.	285.	162.	+33	+ 2
B.	29 " . " .	590.	37.	10 " . " .	325.	106.	+18	-46
C.	1 Jul. '52.	575.	48.	12 " . '52.	280.	85.	-15	-62
C.	15 " . " .	200.	138.	11 " . " .	280.	83.	-31	-40
D.	4 Aug. " .	235.	70.	8 Sept. " .	400.	36.	-48*	-23
E.	5 " . " .	260.	70.	" " . " .	420.	43.	-44*	-46
				Average of all farms.			-28** ± 9.6%	-37** ± 12.5%

* Difference significant with probability of 1 in 20;
** " " " " " " 1 " 100;
(1) Based on analysis of transformed counts.

Worm Egg Counts.

The levels of infestation with *Strongyloides* spp. were low, and this genus was ignored.

Table I gives the dates of dosing, etc., and of the final fæces sampling and weighing on each farm, the initial mean egg counts of the Other Strongyles and of *Nematodirus* spp. for all lambs, the final mean worm egg counts of the control lambs, and the effect of dosing on worm egg yield. Arithmetic means of the actual counts are given to show the general level of infestation in the undosed lambs at the beginning and end of the trial on each farm. The effect of dosing was calculated from the means of the transformed counts, and differences which were statistically significant at $P = 0.05$ (1 in 20) are indicated with an asterisk, and those at $P = 0.01$ with two asterisks.

With the exception of the two tests in 1951, the dosed lambs generally showed a drop in the O.S. egg counts compared with their controls, but the sampling variability was large, so that the difference was only significant on farms D and E. There was also no significant heterogeneity in response to dosing between farms, as judged by a statistical test (see appendix), so there is justification for calculating an average for all farms. This is clearly significant, showing a drop in the O.S. egg count of 28 per cent ± 10 per cent. The picture was the same for eggs of *Nematodirus* spp., since all the trials showed a drop in

the dosed group except on farm A, but none of the individual trials showed a significant effect. There was no significant heterogeneity between trials (see appendix), and the over-all average showed a significant drop of 37 per cent ± 12 per cent. The dosing thus appeared to cause a roughly proportionate drop in the egg production of the Other Strongyles and of *Nematodirus* spp., since the average reductions did not differ significantly.

The later dosings on farms C, D and E appear to cause a relatively greater reduction in the Other Strongyle egg counts than the earlier dosings on farms A and B, but this trend is not significant statistically, neither is it reflected noticeably in the egg counts of *Nematodirus* spp.; therefore it can only be taken as a suggestion that later dosing may be more effective than dosing at the end of June. Moreover, the mean O.S. egg counts were higher at the start of the trials on farms A and B than those of the control groups at the end of the experiments, while on farms C, D and E the O.S. egg counts rose in the control groups during the trials. This fall during July and the rise during August of O.S. egg counts of undosed hill lambs is common to the greater part of Scotland. This different pattern of infestation may possibly account for the difference in the apparent level of the response to dosing on the two groups of farms.

In one trial (farm B in 1951) additional egg counts were made three weeks after dosing. At this sampling the dosed lambs had an average O.S. egg count considerably under half that of the controls, although there was no difference between the two groups a fortnight later. This illustrates the short-term nature of the effect of dosing on the worm-egg counts of these lambs.

Worm-egg counts were made in September or October on many of these lambs at the start of some hogg* dosing trials; during the interval the effect of dosing on the worm-egg counts had been completely lost.

Table II.

Average numbers of larvae of Other Strongyles in cultures of faeces from dosed and undosed control lambs collected four to six weeks after dosing, per 100 larvae identified, and per unit weight of faeces.

	From control lambs,	From dosed lambs,	
	per 100 larvae.	per 100 and per 70 larvae.	
	(col. 1.)	(col. 2.)	(col. 3.)
Trichostrongylus spp.	25	41	28
Ostertagia spp.	60	54	38
H. trigonocephalus	6	3	
H. contortus	5	1	4
Oe. venulosus	4	1	

The numbers of larvae of C. ovina and of Cooperia were so small that they were not included.

Species Involved.

Counts of larvæ from a few cultures of the lamb fæces at the end of the trials suggested that there were some differences in the average output of eggs of the different genera from the dosed and from the control lambs.

* A lamb becomes a "hogg" when it is weaned.

Comparison of columns 1 and 2 in Table II shows that the proportion of eggs of *Trichostrongylus* spp. was increased and that of all others was decreased by dosing, but comparison of columns 1 and 3 suggests that the average actual rates of output of eggs of *Trichostrongylus* spp. was approximately the same in the dosed and in the control lambs. It is not clear whether this indicates that dosing was less successful in eliminating adults of *Trichostrongylus* spp. than those of other genera, or whether there was a fairly complete elimination of all genera, followed by a relatively greater intake of larvæ of *Trichostrongylus* spp.; the second hypothesis is supported by the fact that infestations of *Trichostrongylus* spp. are known to build up at this time of year.

Table III.

Mean lamb weights in pounds, numbers of lambs in samples, and mean (corrected) gain or loss in weight of the dosed compared to the control lambs; the dates are the same as those in Table I.

Farm.	Mean Weights				Sample Size				Mean Loss or Gain in lb.
	Controls.		Dosed.		Controls.		Dosed.		
1951.	Jun.	Aug.	Jun.	Aug.	Jun.	Aug.	Jun.	Aug.	
A.	34.5	50.7	34.6	48.5	23.	26.	23.	22.	−2.4 ±1.1
B.	33.3	48.1	34.3	49.5	24.	24.	24.	24.	+0.1 ±1.1
1952.	Jul.	Aug.	Jul.	Aug.	Jul.	Aug.	Jul.	Aug.	
B.	32.8	46.4	34.3	48.2	24.	24.	24.	24.	−0.1 ±1.1
C.	40.3	47.6	40.3	47.6	34.	36.	35.	34.	0 ±0.9
	Aug.	Sep.	Aug.	Sep.	Aug.	Sep.	Aug.	Sep.	
D.	48.1	52.9	48.3	54.3	36.	35.	35.	37.	+0.7 ±0.6
E.	50.8	58.7	48.8	55.7	30.	30.	31.	29.	−0.5 ±0.7
Average of all farms									−0.15 ±0.34

Body Weights.

Table III shows the mean weights of the dosed and control groups of lambs at the start and end of each trial, the numbers of lambs on which each mean was based, and the effect of dosing on weight, measured as the difference between the final weights of the dosed and control groups after adjustment for initial differences in weight. The slight variations in sample size of some of the groups indicate that in a few cases it was not possible to gather all the lambs of the group at one of the samplings.

On farm A there was probably a significant loss of 2.4 lb. per lamb, as a result of dosing, but no significant change in weight resulted from dosing in any of the other trials; the over-all farms average was -0.15 ± 0.34 lb., so that dosing, in spite of its positive effect in reducing the worm egg counts, appears to have had no effect on body weight, and certainly did not enable the dosed lambs to gain more weight than the undosed lambs. The lambs on farms A and B gained an average of 14 to 15 lb., while the lambs on the other farms, which were weighed a little later, showed much smaller gains of 5 to 7 lb. The trials thus covered a fairly wide range of growth rates, and there was no significant effect of dosing with phenothiazine in causing an increase of weight, whether the growth rate was high or low.

It was possible to follow the growth rate of some of the lambs at a later age to look for longer term effects of the dosings, but, as was to be expected from the absence of immediate effects, no delayed benefit appeared.

Discussion

The only point of importance is whether or not anthelmintic dosing increases the weight of hill lambs; however, worm egg and larval counts help to explain the effect which dosing has had on the worm infestations.

In six trials, phenothiazine in heavy doses caused a reduction in worm egg production, which on most farms, was still evident a month or six weeks after dosing, but did not result in any increased body weight. Phenothiazine caused an immediate sharp drop in worm egg output, but had a progressively diminishing effect as the interval between dosing and worm egg counting increased. After about three months all effect of the dosing on worm egg output had been lost.

Explanations for the disappointing practical results of these trials, which confirm the impressions of many farmers, can, perhaps, be found in a combination of causes.

Crofton (1949) has shown that on the hills of Northumberland larvæ on the grass are numerous after early June, from then they gradually increase in numbers until the end of August, when the number start to decrease again, but they are numerous until the middle of October; therefore, there is little doubt that the lambs were picking up large numbers of larvæ throughout the period of these trials.

In these trials half the lambs were, of course, continuing to spread helminth eggs, but this is unlikely to have increased the number of larvæ on the grass very much. It is typical of Scottish hill grazings that for the three or four months of spring and early summer the ewes and hoggs pass heavily contaminated fæces, and, therefore, the pastures were already heavily infested with larvæ before the start of the trials.

For these reasons, dosing hill lambs might be expected to have a short-lived effect on their worm egg output, but it is surprising that there was no gain in growth-rate, and in one trial an apparent loss of weight. The most probable explanation is suggested by the work of Gordon (1953*a*) who studied the effect on their weight of dosing worm-free lambs with phenothiazine. In one of his trials the lambs dosed with phenothiazine into the rumen and into the abomasum gained an average of over 2 lb. less in the following thirty days than the undosed control lambs; in another trial the average differences were smaller but substantial. Gordon states that there was a loss of appetite in the dosed lambs. The following reports also suggest that dosing with phenothiazine can cause a loss of body weight, as some sheep are adversely affected by this anthelmintic, although in most cases any damage done is masked by the benefit of removing the worm burden. Fethers (1952) in Australia recommended that lambs running with ewes on pasture should not be dosed before three or four months of age; the drenching of lambs or weaners (hoggs) with phenothiazine may cause photosensitisation and result in serious sickness or death occurring between the following day and

three or four weeks later. He also states, " Even when lambs and weaners are not seriously sickened by the drug it is quite obvious that they loathe the taste of it "; this would probably check rumination and reduce grazing; he also writes, " Losses do not appear to be related to the dose rate of the drug, but to some unknown factor affecting the susceptibility of certain individual sheep." Allen and Kyles (1951), reporting on a trial to test a phenothiazine-salt mixture as a growth stimulant for young sheep, which were only lightly infested with *H. contortus, Trichostronglus* spp., *Nematodirus spathiger* and *Strongyloides* spp., found that all the sheep, given the phenothiazine-salt mixture for 25 to 47 days, gained less than sheep to which salt alone was given. The trials were spread over two years, and in both years the average differences were greatest in the trials which lasted over six weeks. The differences were not statistically significant in the first year, but were in the second, when three out of twenty sheep receiving the phenothiazine-salt mixture made gains in weight far below the average. Dunn (1953) has shown that very occasionally phenothiazine may cause slowness in movement and even the death of a Blackface hogg in winter in Scotland; photosensitisation was unlikely and the symptoms did not suggest it. On the other hand Leiper and Peters (1941) reported that small doses of phenothiazine had no effect on the body weight of a few worm-free lambs; and Swales (1940) in a small experiment failed to cause photosensitisation in Cheviot X Border Leicester sheep.

It is interesting that in these trials the biggest check to the dosed lambs was on farm A, where the stock is Scottish Blackfaces, a breed which is probably less likely to suffer from photosensitisation than Cheviots.

It is important that hill farmers should be given correct advice on the choice of anthelmintic and the time at which hill lambs should be dosed. Taylor (1953) has shown the large weight losses in lambs which can be caused by worms; in Scotland the annual hill lamb crop is about two millions, and in England and Wales it is only slightly less. More field trials with other anthelmintics, which have not the disadvantage of phenothiazine, are required. The drugs should be effective against *Ostertagia* spp. in early summer, and also against *Trichostrongylus* spp. later in the season. Because dosing lambs with phenothiazine may produce severe symptoms of photosensitisation (Gordon and Green, 1951) Gordon (1953*b*) recommends the use of copper sulphate-nicotine sulphate for unweaned lambs.

Meanwhile the advice given to farmers varies. Typical recommendations on phenothiazine tins are: " All lambs should be dosed at marking* time, clipping* time (when this is convenient) and at the main summer dipping*. Stock ewe lambs should be dosed in September . . . "; " First at weaning* time and then at monthly intervals "; " Hill sheep should be dosed as a routine when gathered for shearing, dipping, etc., or at least once in the year, preferably towards the end of summer," and " When the lambs are eight weeks old, give each lamb 1 fl. oz. . . . repeat the above doses for lambs and sheep monthly."

* Marking time is in late May or early June (the lambs are under two months old); clipping time is in late June or early July; the summer dipping is usually in late July or August, and weaning time is in the last half of August or early September on most hill farms.

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Greig (1951), advising dosing times for hill sheep, says " . . . and the whole flock may be treated at marking time. Treatment is repeated at clipping time or at the summer dipping, at weaning time, and . . . "

The suggested dosing programmes for hill sheep seem to have been based mainly on experience with lambs in fields, but the results given in this paper suggest that dosing of hill lambs with phenothiazine should only be resorted to when it is clearly necessary, or on farms where it has been proved to do good.

Any criticism, however, of the use of phenothiazine for dosing Scottish hill lambs does not imply condemnation of the use of phenothiazine for dosing hoggs, which benefit considerably from dosing at the right times.

Summary

Dosing trials with phenothiazine were carried out on hill lambs on five farms in Southern Scotland during 1951 and 1952. The lambs were dosed in late June or early July on three farms, and in early August on the other two, and the changes in the worm egg counts and body weights after about five weeks were compared with the corresponding changes in undosed lambs run together with the dosed lambs.

There were no significant differences between farms in response to the dosings; output of Other Strongyle eggs was on an average 28 ± 10 per cent lower and of *Nematodirus* spp. eggs 37 ± 12 per cent lower as a result of dosing. The dosed lambs showed no tendency to gain weight more rapidly than the undosed lambs.

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Statistical Analysis

By E. C. R. REEVE*

Worm Egg Counts.

Analysis of data on worm egg counts presents an awkward, but important, statistical problem since the frequency distribution is generally skew, cut off sharply by zero at the lower end and having a long tail at the upper end. The

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sampling variance also tends to increase as the mean increases. Hunter and Quenouille (1952) have suggested fitting a negative binomial distribution, but this raises difficult problems of estimation, and for our purpose it seems best to transform the data to make the distribution more nearly normal and to eliminate most of the correlation between mean and variance. The transformation $y = 100 \log_{10} (x + 1)$ was found satisfactory, where x is the number of eggs counted in four cells of the McMaster worm egg counting slide (50x is the number of eggs per gm. of fæces), and the factor 100 is used to move the decimal point to a more convenient position for computing. The constant 1 is added to all counts to enable counts of zero to be included without being faced with log 0. It would be a little better to add $\frac{1}{2}$ instead of 1, when the mean count is low, but 1 was used in order to make the analysis comparable to other (unpublished) results. The following analysis was made on the transformed variate (y).

Each trial consisted essentially of two random samples of lambs measured immediately before dosing and a month or more afterwards. The question arises how far differences between the means of the dosed and the control groups at the start of each trial will effect the final differences, i.e., what is the regression coefficient of final worm egg count on initial count, within samples. This can only be calculated for the trials on farm B, where it was alone possible to mark lambs for individual identification, and the regression coefficients with their standard errors obtained from these trials are given in Table IV, which shows also the corresponding analysis for body weight.

Table IV.
Regression of final on initial transformed worm egg count (y) and of final on initial body weights.

Farm B.	Other Strongyles.	Hæmatodirus spp.	Body weight.
Controls, 1951,	−0·183 ± 0·23	−0·127 ± 0·29	1·26 ± 0·20
" , 1952,	−0·025 ± 0·24	+0·434 ± 0·25	1·27 ± 0·08
Dosed, 1951,	−0·140 ± 0·24	+0·016 ± 0·28	1·53 ± 0·10
" , 1952,	+0·103 ± 0·17	−0·191 ± 0·19	1·14 ± 0·09
Average,	−0·062 ± 0·11	+0·006 ± 0·12	1·30 ± 0·06

None of the regression coefficients for either group of worm eggs differs significantly from zero, and the averages are so small (−0.062 ± 0.11 for O.S. and +0.006 ± 0.12 for N.) that initial differences cannot have any appreciable effect on the final differences. These figures relate only to one farm, but they are consistent and it seems unlikely that other farms will show much correlation over the period concerned. It has, therefore, been assumed that initial differences in worm egg counts, which were not usually large, can be ignored in calculating the effect of dosing.

The variances of the transformed worm egg counts and of body weights are shown in Table V. The control and dosed groups differed little in variance, and have been pooled, as have the variances for individual hefts where more than one was used on a farm.

The variance of O.S. is rather higher on farms A and B than on the others,

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while there appear to be three levels of variance for N., on farm A, farms B and C, and farms D and E. The averages for these groups are shown at the foot of the table and have been used in calculating the standard errors for the different trials, since they are probably rather more reliable than the individual estimates.

Table V.

Variances of transformed final worm egg counts (y) and of body weights. Pooled variances of hefts and of dosed and control groups.

Farm.	Degrees of Freedom.	Variances.		
		O.S.	N.	Body weight.
A.	43	1500	1200	60
B, 1951.	45	2100	860	101
", 1952.	46	1400	770	64
C.	68	1000	680	59
D.	63	1200	360	26
E.	49	800	470	37
Averages		A & B. 1700 C to E. 1000	A. 1200 B & C. 770 D & E. 410	A to C. 70 D & E. 31

* For body weight, the degrees of freedom are Farm D: 66, E: 55.

Comparing the variances of Table V with the means of Table VI, there is some correlation remaining between the mean and variance for N., but none for O.S. This correlation doubtless arises because of the low mean counts of N. on farms D and E, since the transformation is not completely effective at these low levels. With the higher levels of output of O.S. eggs, it appears to eliminate completely any correlation between the mean and variance.

The standard error of the difference between the mean worm egg counts of the dosed and controls is calculated as the square root of $\frac{V}{d} + \frac{V}{c}$ where where V is the variance from Table V, and d and c are the sample sizes of the

Table VI.
Effect of dosing on transformed worm egg counts (y).

Farm.	Final mean count of controls.		Effect of dosing: Dosed - Control mean.	
	O.S.	N.	O.S.	N.
A	64·0	51·1	+ 9·6 ± 12·0	+ 1·0 ± 10·5
B, 1951.	65·9	39·2	+ 6·3 ± 12·0	-13·9 ± 8·1
", 1952.	64·4	30·8	- 5·4 ± 12·0	-16·5 ± 8·1
C.	73·1	34·5	-12·6 ± 7·6	-11·0 ± 6·7
D.	81·8	15·5	-21·0 ± 7·6	- 3·8 ± 4·8
E.	98·0	19·1	-20·2 ± 8·8	- 8·0 ± 5·4
		Overall average	-11·2 ± 3·8	- 7·9 ± 2·7

dosed and control groups. Table VI gives the means of the transformed counts and their difference with its standard error, for each farm, together with the weighted averages for all farms. The estimates of dosing effect in Table I were

obtained by converting back the means of Table VI and expressing their difference as a percentage effect.

An approximate test of heterogeneity in the response to dosing on the different farms may be made by treating the mean differences of Table VI, each weighed by the reciprocal of its variance, as χ^2 variates, and separating the variance between farms into parts attributable to the average response and to differences between farms. Taking z as the mean difference and w as the reciprocal of its squared standard error, the analysis is made as shown in Table VII.

Table VII.
Test of Heterogeneity in response to dosing.

Nature of effect.	Formula.	Degrees of freedom.	Other Strongyles.		Haematodirus spp.	
			χ^2	P.	χ^2	P.
Average response.	$(\Sigma wz)^2/\Sigma w$	1	8.6	<0.01	8.8	<0.01
Heterogeneity.	$\Sigma wz^2-(\Sigma wz)^2/\Sigma w$	4	7.6	0.1	3.4	0.5

P gives the probability of exceeding the values of χ^2 by chance. While the average response to dosing is clearly significant for both O.S. and N., there is no evidence of heterogeneity between farms; i.e., if there are any real differences between farms they are not great enough to show up in view of the rather small samples and high sampling variability.

Body Weight.

In the case of weight no transformation is necessary, but initial weight differences between the dosed and control groups must be expected to affect the final comparisons. The last column of Table IV shows that, on Farm B, each 1 lb. difference between two lambs in their initial weights led, on an average, to 1.3 lb. difference at the final weighing. This change is roughly proportional to the change in weight during the trials, so that heavy and light lambs appear to have grown at approximately equal percentage rates during the period of the trials. It is unlikely that the regression coefficient will vary much from farm to farm, since the trials only lasted for four to six weeks, and minor variations will not have an appreciable effect on the analysis. The effect of dosing on weight is therefore estimated as: $D_f - C_f - 1.3(D_i - C_i)$ where D and C are the dosed and control mean weights, and subscripts i and f indicate the initial and final weighings.

The correction for differences in initial weight reduces the variance of the final weight difference in the proportion $1:(1 - r^2)$, where r is the correlation between the initial and final weights of the same lamb, calculated within samples. The correlation coefficients for the four samples on farm B, in the order given in Table III, were 0.81, 0.96, 0.95, and 0.94, giving a mean of 0.93, so that $(1 - r^2)$ is 0.14. This value has been increased a little to 0.2, in order to allow for the small additional errors due to the occasional failure to weigh all lambs in the group.

The variances of the dosed and control groups did not differ significantly,

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and have been pooled in Table V. Farms D and E had rather lower variances than the others, and the values for A to C, and D to E have been averaged separately. The standard errors of the corrected weight differences, quoted in Table III, were calculated as: Standard error = square root of $0.2\left(\frac{V}{c}+\frac{V}{d}\right)$ where V is the appropriate average from Table V (i.e., 70 for farms A to C, and 31 for farms D and E), and c and d are the numbers of lambs in the control and dosed groups at the final weighing.

These standard errors should be taken as approximate only, in view of the margins of uncertainty in the factor $(1 - r^2)$ and in the regression coefficient. A test of heterogeneity in the weight differences for the different farms could be made, but it is obvious from the differences and their standard errors, shown in Table III, that no significant heterogeneity would be found.

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CHLORAMPHENICOL (CHLOROMYCETIN) AND FOOT-ROT IN SHEEP

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THIS paper describes observations on the use of Chloromycetin, in 2.0 per cent and 0.5 per cent alcoholic solutions, in the treatment of contagious foot-rot in sheep under field conditions.

The term " foot-rot " in this paper is used to mean the disease which affects the deep tissues under the horn and sole of the foot causing separation of the horn and is accompanied by extreme lameness. The disease has been described by Beveridge (1935, 1938, 1941) and attributed by him to certain causal organisms acting together, particularly *Fusiformis nodosus* with *Spirochæta penortha* and a species of motile fusiform bacterium. This type of foot-rot is sometimes observed in the interdigital cleft, but whatever the site, it is always accompanied by a characteristic offensive odour. No attempt has been made in this experiment to treat any of the other forms of " foot-rot," some of which may be due to infection with pyogenic bacteria, particularly *Corynebacterium pyogenes* or to infective agents which more usually affect the coronet or other hair-covered portions of the leg. The pyogenic form produces great heat, extensive swelling, lameness and an offensive odour but the latter is not the characteristic odour of the more common form in which heat and swelling are also less in evidence. The coronet or leg form, described by Harriss (1948), produces no characteristic odour and usually little or no lameness.

Stewart (1954) reported that the strain of *F. nodosus* tested by him was highly sensitive to penicillin (500 units per ml.) and to chloromycetin (5.0 mg. per ml.).

Working under laboratory conditions, Stewart (1954) compared 10 per cent chloromyctetin in propylene glycol with various other medicaments and antibiotics. Striking results were obtained in two feet treated with chloromycetin. Subsequently, in a series of five tests under field conditions involving 12, 12, 12, 24 and 25 sheep respectively, he claimed cures of 81 to 100 per cent for 10 per cent chloromycetin either in methylated spirits or propylene glycol, 41 per cent cures with 2 per cent in methylated spirits, and 50 per cent cures with 5 per cent in methylated spirits. In most cases a single application of the antibiotic was used but some feet received a second application. Stewart was able to hold his treated sheep on slatted floors typical of Australian woolsheds. This procedure could undoubtedly influence the efficacy of the treatment. He estimated that one pint of 10 per cent chloromycetin solution would be sufficient to treat 250 to 300 feet, implying an approximate cost of one shilling per foot treated. In an endeavour to reduce the cost of treatment it was decided to investigate the efficacy of 2.0 per cent and 0.5 per cent solution of the antibiotic in methylated spirit. In this trial it was estimated that one pint of solution would be sufficient to treat 20 sheep, bearing in mind the possibility

that more than one foot of each animal may be affected. In practice this quantity of solution, used under the practical conditions of sheep yards, proved barely enough for the purpose.

Sambrook (1955) reported that 30 rams, suffering from advanced foot-rot, were cured after use of 10 per cent alcoholic solution of chloromycetin applied on three occasions at intervals of five to six days. These rams were penned for one hour after treatment until the feet were dry.

The Flock

There was available at this establishment a flock consisting of some 600 sheep of various ages and of various breeds, chiefly Clun, Hampshire Down, Wiltshire Horn, and Wilts/Hants cross-breds, Oxford/Clun cross-breds, and other cross-breds of unknown origin. Lameness was very prevalent and it was decided to attempt to eliminate the infection of "foot-rot" by the familiar process of isolation of infected sheep, resting infected pastures for 14 days and a general foot bath treatment for all other sheep.

Time of Year

The programme of elimination was timed to start about the middle of August, shortly after weaning the lambs, and this gave a period of six weeks before the first of October when the rams were put out.

Method

1. Every sheep in the flock was turned-up and its feet examined but not trimmed. Any showing even slight foot-rot were removed. Ninety-nine sheep, including 15 lambs, were found to be affected.

2. The affected sheep were caught and their feet pared with foot-rot shears till all diseased tissue was exposed. Paring was done carefully and diligently and the worst cases were treated quite ruthlessly.

3. Each sheep (ewe or lamb) was put in one of the three following treatment groups in successive order and without selection:

Group 1 had all diseased feet painted with 0.5 per cent Chloromycetin solution.

Group 2 had all diseased feet painted with 2.0 per cent Chloromycetin solution.

Group 3 received no immediate treatment.

Painting was done with a stiff bottle brush to assist penetration.

4. After treatment the sheep were stood in a yard for approximately half an hour to two hours to enable the Chloromycetin to have its effect before dilution in the foot bath. (It was unfortunate that this experiment had to be carried out in open yards, and the unusually wet August and September of 1954 provided scant opportunity for the feet of the sheep to remain uncontaminated with mud or slush.)

5. All sheep were then passed through a bath containing 10 per cent Copper Sulphate to disinfect untreated feet. It was impracticable without the

use of special boots to prevent feet treated with Chloromycetin being immersed in the Copper Sulphate, but as the test was intended to show the practical use of Chloromycetin, this method seemed the most reasonable.

6. The three groups were taken separately, either by driving or by mechanical transport, to three fresh paddocks which had not contained sheep for several months previously.

7. Each group was mustered on its own field at intervals of a week to ten days. All feet were examined and affected feet were trimmed to expose any active foci of disease. The progression or regression of the disease was estimated in each case and according to the following table was classified either P, Q or R. P = cured; Q = healing well; R = little or no improvement.

On the first five examinations, active lesions were treated according to the plan of treatment indicated under 3, thereafter, after examination and trimming, the sheep were passed through a footbath containing 10 per cent copper sulphate.

Results

These are set out in tabular form below:

Table 1

Group	1			2			3		
Per cent Chloromycetin	0.5			2.0			Nil		
Sheep in Group	33			33			33		
No. of feet involved at 20. 8. 54	52			48			47		
Classification*	P	Q	R	P	Q	R	P	Q	R
1. 9. 54	2	20	11	8	16	9	6	9	18
8. 9. 54	5	20	8	14	16	3	14	9	10
15. 9. 54	13	13	7	14	10	9	20	7	6
22. 9. 54	18	11	4	23	9	1	24	5	4
29. 9. 54**	23	5	5	30	2	1	25	4	4
4. 10. 54	26	3	4	30	2	1	27	2	4
14. 10. 54	27	3	3	30	2	1	27	2	4
26. 10. 54	28	2	3	31	1	1	28	1	4

* P = cured, Q = healing well, R = little or no improvement.
** Last treatment with Chloromycetin.

It was apparent to the operator that there was a better response after the first two dressings to the stronger (2 per cent) solution of Chloromycetin than to either the weaker (0.5 per cent) solution or to 10 per cent copper sulphate solution alone, but after further dressings there was little to choose between the various treatment groups.

Statistical analysis of the results (3 x 3 table for each examination) after 12, 19, 26 and 33 days respectively, confirmed this impression and the conclusion was reached that Group 2 (2 per cent chloramphenicol) responded significantly better to treatment in the first and second weeks $\frac{\chi^2}{4} = 11.2$ (Prob. = 2 per cent

approx.) at 12 days, and $\frac{\chi^2}{4} = 12.8$ (Prob. = 1 per cent approx.) at 19 days. In the third and fourth weeks there is no significant difference.

Statistical Analysis

1. 9.54 (12 days)

	1	2	3	Total
P	2 (5⅓)	8 (5⅓)	6 (5⅓)	16
Q	20 (15)	16 (15)	9 (15)	45
R	11 (12-2/3)	9 (12-2/3)	18 (12-2/3)	38
	33	33	33	99

$\frac{\chi^2}{4}$ = 11.1 (Prob. = 2 per cent approx.)

8. 9.54 (19 days)

	1	2	3	Total
P	5 (11)	14 (11)	14 (11)	33
Q	20 (15)	16 (15)	9 (15)	45
R	8 (7)	3 (7)	10 (7)	21
	33	33	33	99

$\frac{\chi^2}{4}$ = 12.8 (Prob. = 1 per cent approx.)

15. 9.54 (26 days)

	1	2	3	Total
P	13 (15.2/3)	14 (15-2/3)	20 (15-2/3)	47
Q	13 (10)	10 (10)	7 (10)	30
R	7 (7⅓)	9 (7⅓)	6 (7⅓)	22
	33	33	33	99

$\frac{\chi^2}{4}$ = 4.3 (Prob. = 35 per cent approx.)

22. 9.54 (33 days)

	1	2	3	Total
P	18 (21⅓)	23 (21⅓)	24 (21⅓)	65
Q	11 (8⅓)	9 (8⅓)	5 (8⅓)	25
R	4 (3)	1 (3)	4 (3)	9
	33	33	33	99

$\frac{\chi^2}{4}$ = 5.2 (Prob. = 25 per cent approx.)

Disregarding the efficacy of the forms of treatment, the results show that the prevalence of foot-rot in affected sheep can be reduced within four to five weeks to about 10 per cent of the original total. Further treatment, with 10 per cent copper sulphate, no matter how carefully applied, fails to clear up the remnant (which can be considered as chronic carriers). Whether these cases

could be cured by further treatment with antibiotics remains for further study, but, under ordinary field conditions, it would seem that the proper course would be to discard these sheep from the flock for slaughter. It has not been possible in this study to observe the effect of Chloromycetin alone as it was necessary to pass the sheep through a copper sulphate foot bath before turning out on to clean pasture.

Discussion

The claims of Stewart (1954) and Sambrook (1955) that 10 per cent alcoholic solution of Chloromycetin can produce remarkable cures for foot-rot in sheep, have prompted the tests, described in this paper, to see if a concentration of less than 10 per cent could be equally successful. It would appear, therefore, that the cost of 1s. per foot treated, which is the figure quoted by the manufacturers of Chloromycetin, when 10 per cent alcoholic solution is used, would involve a total cost, on Sambrook's basis of three or four treatments, of 3s. to 4s. per foot treated. Reference to Table I shows that the average number of feet involved is 1.5 per sheep. The average expenditure per sheep is therefore approximately 5s. Attempts to reduce this cost by the use of a concentration of 1/5th or 1/20th of that used by Stewart and Sambrook have not proved successful.

Summary

The application to affected feet of Chloromycetin, in concentrations of 1.0 per cent and 0.5 per cent in alcoholic solution, possesses no advantages over 10 per cent copper sulphate solution as a foot bath.

In the absence of a treatment more successful than copper sulphate foot baths, the continued treatment of foot-rot after a month has elapsed results in few further recoveries and such sheep are best eliminated from the flock.

Acknowledgments

My thanks are due to Dr. J. S. Paterson for his interest and for acting as an independent witness in the examination of the treated feet, and to Mr. S. Peto for examining the results statistically. Acknowledgment is made to the Chief Scientist, Ministry of Supply, for permission to publish this communication. I also wish to record my thanks to Messrs. Parke, Davis & Co. for the supplies of Chloromycetin used in this experiment.

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TERRAMYCIN AND FOOT-ROT IN SHEEP

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THE observations on the treatment of the most common form of foot-rot in sheep as described by Beveridge (1941) has, in recent years, provided considerable evidence that 10 per cent chloromycetin is more efficient than copper sulphate solution, though it is doubtful if the footbath can be dispensed with as a prophylactic measure (Stewart, 1954; Sambrook, 1955; Harriss, 1955). The observations of these workers indicate that a 10 per cent tincture is efficacious but relapses follow the use of 2.0 per cent tincture.

This paper describes a preliminary trial to ascertain whether terramycin, which is now available, is a useful agent for the treatment of foot-rot in sheep. The manufacturers of terramycin claim that foot-rot in sheep due to *Fusiformis nodosus* and other species of fusiformis, responds to treatment and that the antibiotic has also proved effective in the treatment of foul-in-the-foot in cattle.

The Flock

The flock available for the trial has already been described (Harriss, 1955). Foot-rot had not been eliminated despite constant footbath treatments (10 per cent copper sulphate), and latterly by 2 per cent chloromycetin. The present observations were carried out in mid-winter. Most ewes were heavy in lamb and the conditions underfoot, after a very wet summer and autumn, were most unfavourable to the animals.

In view of the conditions generally and the state of the existing sheep yards, a set of hurdle yards were constructed on a concrete apron. During the course of the experiment these temporary yards were soiled constantly by dung and urine but they drained well and the sheep stood free of slush.

Methods

The preliminary treatment and division of animals into three groups were identical with those already described by Harriss (1955). The number of sheep found affected consisted of 54 ewes and three lambs.

The treatment of the three groups, which each consisted of 19 sheep, was as follows:

Group 1. Affected feet were pared and treated with terramycin and protected by waterproof boots. Unaffected feet were treated with copper sulphate in a footbath.

Group 2. No treatment after paring other than 10 minutes in a 10 per cent copper sulphate footbath.

Group 3. No treatment to affected feet after paring. Boots applied and unaffected feet treated in 10 per cent copper sulphate footbath.

Care was taken to ensure that boots smeared internally with terramycin (Group 1) were not used for animals in Group 3.

Treatment

The antibiotic was used in the form of an ointment containing 5 mg. terramycin and 10,000 units Polymycin B Sulphate per gm. The pared foot was wiped clean in an attempt to remove as much moisture and blood as possible. A small quantity of ointment was squeezed out of the tube and rubbed in with the finger. In practice, a one-ounce tube was found to be sufficient to treat 30 to 40 feet. After treatment the treated feet were booted and the sheep were passed through the copper sulphate footbath and held in the concrete yards for at least one hour. Boots were removed on leaving the footbath.

After treatment the sheep were driven to the single available pasture where all three groups were held together.

At intervals all feet were examined, trimmed where necessary, and the progression or regression of the disease classified as follows:

P = cured
Q = healing well
R = no improvement or even deterioration.

On account of the time of the year (December) more attention was paid to the health of the sheep prior to lambing than to the purely academic interest in the merits of any particular antibiotic in the treatment of foot-rot. It was therefore necessary, even at the second examination of the feet, to use the antibiotic on the group which had not been treated in this manner, and after the fourth examination, on the group which had been treated with copper sulphate only. The experiment concluded on 3.3.55 as the ewes had started to lamb. Results are set out in Fig. 1.

Fig. 1

Group	1			2			3		
Treatment	Terramycin + Boots			Copper Sulphate No Boots			No Treatment + Boots		
Sheep in Group	19			19			19		
No. of feet involved at 22.12.54	29			30			27		
Classification[a]	P	Q	R	P	Q	R	P	Q	R
31.12.54	11	7	1	9	5	5	9	2	8
							Terramycin applied without footbath		
13. 1.55	15	3	1	9	4	6	13	4	2
9. 2.55	17	-	2	11	1	7	18	1	-
				Terramycin applied without boots					
3. 3.55	19	-	-	16	1	2	19.	-	-

[a] P = healed
Q = improving
R = no improvement and/or progressive deterioration

Discussion

It was evident at the first examination, nine days after the initial treatment, that the feet of the group which had received an application of terramycin were in much better condition than either of the other groups. The group which had received no treatment had many feet in which the disease was actively progressing. This group was therefore treated for the first time with terramycin. At the next inspection an improvement was obvious and this continued until at the fourth inspection all the feet in this group and in group 1 had completely recovered. It was noted that little beneficial progress was being made in the group treated in the copper sulphate footbath. After the third inspection, terramycin was used on this group also and at the last and final inspection of these sheep encouraging results were observed.

We have found that in use, one tube will treat 30 to 40 feet and that the average infection rate is 1.5 per sheep, so that one tube will treat 20-30 sheep. or an average of 25 sheep. Based on the present professional price, the cost of treatment is therefore about 2½d. per sheep at each application.

The use of an ointment instead of a tincture presents certain advantages. Under practical conditions the ointment in tube form is unspillable and easily portable. When applied to the foot it is less likely to suffer dilution by water and mud than a tincture, whilst it is more likely to act as a barrier between moisture and the sensitive tissues of the foot. Its application requires no brush or other instrument.

No attempt has been made to determine if the footbath is necessary for the disinfection of unaffected feet. It is possible that it still has a place in the control of foot-rot, but it remains to be determined if the footbath and terramycin ointment can be used in conjunction with each other.

Summary

The application of terramycin in the form of an ointment containing 5 mg. of terramycin and 10,000 units of Polymyxin B Sulphate per gm. was found highly effective against the common form of foot-rot in sheep. The cost is estimated at about 2½d. per sheep at each application.

Acknowledgments

My thanks are due to Dr. J. S. Paterson for his interest and advice, and to Messrs. Pfizer Ltd. for generous supplies of terramycin ointment. Acknowledgment is made to the Chief Scientist, Ministry of Supply, for permission to publish this communication.

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ANTHRAX—THE CARRIER STATE IN GOATS

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SEVERAL observers have been under the impression that goats can harbour anthrax organisms without suffering from clinical disease and that such animals may die suddenly from anthrax after exposure to severe climatic conditions or the pyrexia following the inoculation of goat-adapted rinderpest virus. The following experience shows that, at least under experimental conditions, such a carrier state may exist.

Anthrax vaccine is prepared from Sterne's strain 34 F_2 and by his method (Sterne, 1946). The concentrated suspension is tested in guinea pigs and the final vaccine in goats. Indigenous strains used as spore suspensions in 50 per cent glycerine are used for testing the immunity in goats and the strain used in the test detailed below had never previously been used for this purpose. It had been isolated from cattle some years ago in an outbreak of anthrax which followed from the use of "wet" goat-adapted rinderpest virus vaccine in Gwandu Emirate, Northern Nigeria. "Wet" goat virus rinderpest vaccine is now obsolete and it is only used in cases of extreme necessity.

In order to assess the virulence of the Gwandu strain before using it for challenge a dilute spore suspension in 50 per cent glycerine was inoculated into Kano brown goats with results as follows:—

Group 1:

Goat No. 7: 1 cc. of 1/10 dilution subcutaneously.
Died in 5 days with anthrax.

Goat No. 8: 1 cc. of 1/100 dilution subcutaneously.
Survived.

Goat No. 2: 1 cc. of 1/1000 dilution subcutaneously.
Died in 8 days with anthrax.

This was an anomalous result as local goats had been found previously to be, without exception, very susceptible. The value of the vaccine was then tested using 1 cc. of 1/10 dilution of the Gwandu strain spore suspension, as a challenge. The results were as follows:—

Group 2:

Goat No. 48	Non-vaccinated controls	All received 1 cc. of 1/10 dilution of *B. anthracis* (Gwandu)	D.3
Goat No. 4			D.5
Goat No. 50			D.7
Goat No. 17	Vaccinated three weeks previously		S.
Goat No. 40			S.
Goat No. 9			S.

D.3 = Died in 3 days.
S. = Survived.

After three weeks in quarantine the four surviving goats were dismissed from the experiment in a normal state of health and were brought into a box in the stables near the main building.

Goat No. 8 died 47 days after being inoculated and the diagnosis of anthrax was made by blood smears and was confirmed by guinea pig scarification. The surviving vaccinated goats which remained were immediately moved back into quarantine and all three were apparently in good health. Goat No. 17 died 51 days after challenge and again anthrax was confirmed.

Discussion

It was considered most unlikely that the deaths of these two goats from anthrax were due to a natural infection of *B. anthracis*. Both had received a challenge of virulent organisms and one had been vaccinated. No case of anthrax had been recorded in the buildings in which Goat No. 8 died and no spontaneous case has been observed in the isolation pen.

It is known that the killing power of *B. anthracis* is associated with the growth of the organism in the tissues of the host (Keppie, *et al.*, 1953). De Moulin and Soemanegara (1937) showed that the bacilli became avirulent within a few days in rabbits which were infected with virulent material, but which failed to die. It therefore seems probable that in these two goats the inoculated spores remained " dormant " in the tissues. In fact, this is the only explanation which would allow for the presence of this virulent strain of *B. anthracis* in the long period between inoculation of the spores and the deaths recorded, as there was no question of chronic disease. Such an infection is well known among the anaerobic, spore-forming organisms. (See Jamieson, 1949.)

Certain animal tissues constitute the natural habitat of *B. anthracis* and some stimulus is probably necessary for development: the products of inflammation may well be the activating agent required as inflammation is known to influence both virulence and immunity (Sterne, 1948). The damage to the dermis by the needle may have been nullified by gravitation of the inoculum from the site. Strains causing aberrant or delayed reactions occur naturally and Gambles, R. M. (1938) cites an instance in Cyprus of a delayed reaction of 22 days in a goat given 1 cc. of 1/10,000 dilution of virulent spore suspension.

The difference between a delayed reaction, however, and the carrier state is a fine one and it would be difficult to differentiate between the two. A goat with a delayed reaction of two months or so may be described as a " carrier " and such a carrier state might explain the cases of intercurrent infections of anthrax which are seen in the field.

Summary

Two Kano brown goats, one of which had been vaccinated, died from anthrax 47 and 51 days respectively after having been given a spore suspension of *B. anthracis*. In the interim period they appeared to be in good health and it is postulated that, when such instances occur under natural circumstances, they explain the cases which are seen in which anthrax appears to occur as an intercurrent infection.

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REVIEWS

GENETIC HOMEOSTASIS, by I. M. Lerner, 1954. Pp. 134. Edinburgh: Oliver and Boyd. Price 12s. 6d.

PROFESSOR LERNER defines genetic homeostasis as "the property of the population to equilibriate its genetic composition and to resist sudden changes" and in this excellent monograph, he develops, and gives some convincing evidence to support this thesis. The basic theory of Lerner's hypothesis is that natural selection favours individuals which are well canalised—that is, those which possess auto-regulating buffering powers to stay within normal channels of development.

Though the treatment of the subject is such that the student of genetics will find it of most value, the author has looked at his subject from the point of view of the worker on animal improvement rather than as a naturalist. This will greatly increase the number of readers who will benefit from studying this book. An excellent bibliography is given at the end.

Finally, one must congratulate the publishers on producing the book so well, and at such a reasonable price.

NICKEL-SCHUMMER-SEIFERLE, LEHRBUCH DER ANATOMIE DER HAUSTIERE, Band I: Bewegungsapparat, 1954. Berlin: Paul Parey Verlag. Price DM.78. (In German.)

THIS is the first part of a work that will eventually be completed in three volumes. The present volume deals exclusively with the osteology, arthrology and myology of the domestic animals and when it is noted that it contains no less than 518 large pages and 517 figures it will be realised that the work is conceived on an impressive scale. It is with surprise, therefore, that we note the author's insistence that it is designed as a textbook and not as a work of reference: one must assume that the German student of to-day has inherited his share of Teutonic thoroughness—and, incidentally, must be a man of means since the first volume alone costs over £7 in this country.

Outside the German-speaking countries this book will have a specialised appeal and must, despite the authors' disclaimer, be considered in this light. Many veterinary anatomists had hoped that this work would fill the gap left by the passing of Ellenberger Baum: they will be disappointed, for despite its length,

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the present work appears to be less detailed and the almost complete absence of references is a serious drawback. The plan of the book is interesting, each section being introduced by a lengthy comparative survey with many allusions to the anatomy of man as well as of domestic animals, after which come the special sections on the dog, the ruminants, the pig and the horse. The order of species is of interest and the horse coming last appears to be dethroned from the place of pride it has occupied for so long.

The text is readable and includes much more of functional interest than has been customary in works of veterinary anatomy: for example, there are considerable discussions on the group actions of muscles and the different gaits of the several animals. Where consulted on points of detail the account is accurate and lucid if it answers the question at all, but many places are less detailed than one would expect. Several important topics are described sketchily: for example, inadequate treatment is awarded to the sinuses of the skull of the horse and to the movements and articulations of the spine: indeed, the entire treatment of the joints is surprisingly sketchy.

The illustrations are very numerous but of uneven quality: many are excellent but many others, obvious copies of familiar illustrations from other works, are poor. The production is beyond praise—printing and paper are superlative and fully maintain the best pre-war standard of German scientific works.

DOGS, CATS AND PEOPLE, by Norman Comben, B.Sc., M.R.C.V.S.. London: Thames & Hudson. Price 15s. net.

A VETERINARY SURGEON'S life is replete with humour, pathos and adventure. No two jobs or set of circumstances are exactly the same. There is something new or unusual around every corner, and no doubt it is these factors which add spice to his life and tends to the "talking of shop" whenever two or three gather together.

Comben's book details the incidents in the life of a town practitioner, and deals only with "small animal" practice. The author did not buy an established business but adopted the heroic way of putting up his plate. His story reveals how successful this method can be if one selects the right district or site and is prepared to give real service. He pays tribute to the value of new therapeutic agents, the sulpha compounds, the antibiotics, and modern methods of anæsthesia which collectively have made veterinary medicine and surgery safe and efficient. Many of his incidents are commonplace in any practice but he tells them with a verve that the most blasé practitioner can read them and chuckle. In other chapters he reveals the troubles and trials of a large quarantine station, he gives a very good account of the Greyhound Racing industry, and he takes us also amongst the "wide boys" of Club Row who prosper on the gullibility of the sentimental members of the public. His chapter dealing with the canine hierarchy and the Kennel Club reveals the tremendous hold that the dog has achieved upon his British master, and the elaborate steps that the latter has taken to ensure that his friend shall not fail in type, form or parentage. I am glad that he has not ignored the cats who

grace our hearths, bear our favours with supreme insouciance, and seek their pleasures in the back-garden night clubs.

His remarks on "Animal Welfare" and those who practice this art are well informed, constructive, and yet subtly critical.

Most veterinary surgeons will enjoy this book. It will appeal also to all those who are interested in Dogs, Cats, and the vagaries and psychology of their owners.

ITEMS OF VETERINARY INTEREST

NEWMAN NEAME, LTD., have designed and produced an interesting illustrated account of the work of Chappie, Ltd., of Melton Mowbray, manufacturers of cat and dog foods.

"Cats, Dogs and Diets" is designed for circulation among veterinary surgeons and students, and distributors of pet foods, with the object of promoting the company's products.

The contents are divided into five chapters. There is a foreword by Captain T. L. Wright, M.R.C.V.S., Hon. Veterinary Surgeon to H.M. The Queen. The first chapter deals with the company's emphasis on scientifically balanced and attractive animal diets. The next two chapters describe the chief ingredients of the company's pet foods—liver, whalemeat, herring and whitefish—how these are obtained and hygenically processed in the company's factory. This is followed by a review of the laboratory and consumer research undertaken to ensure the highest level of quality and acceptability for their products. The final chapter is devoted to general notes on the feeding of pets.

THE first number of "Veterinary Reviews and Annotations" is to hand. This is a new journal to be published annually in two parts by the Commonwealth Agricultural Bureaux. It is their aim to include original review articles on subjects of topical interest. This first issue contains, in 54 pages, papers by Professor R. Lovell on intestinal diseases of young calves, C. Horton-Smith on coccidial parasitism, and Phyllis G. Croft on euthanasia. The subject matter of these articles is condensed, well presented and readable and authoritative reviews of this kind should be of value to veterinary surgeons and research workers who find difficulty in keeping in touch with the vast amount of veterinary literature now in circulation. It should also be of assistance to students though the cost of 25s. may be considered prohibitive by this "lower income" group.

ECHO FROM THE PAST

(*From the* VETERINARY JOURNAL, *May*, 1880.)

CORRESPONDENCE.

Unmitigated Quackery.

Dear Mr. Editor,—Knowing your affection for the animal creation, and your general desire to promote the universal happiness of mankind, I feel no apology is needed in handing you the enclosed card. Should it (the card)

or its author's audacity make you burn please note that the lotion is an antidote. England the enlightened most undoubted must patronise such charlatanism, else it would not exist.

Is the aristocrat or the plebeian the most staunch supporter?

Yours sincerely,

London 14/4/'80. "ANTI-PSEUDO," SENIOR.

CHARLES CROSS, HORSE AND DOG DOCTOR,

2 Gray St., Oxford St., London,

Respectfully informs the Nobility, Gentry and the Public in general that having had many years' experience in the above business, he can undertake the effectual removal of Warts or Wens from Cattle and Dogs by the use of a preparation known only to himself. He can also supply an infallable Lotion for Wrenches and Sprains, Sore Backs and Wrung Shoulders in Horses. This Lotion is likewise an excellent remedy for Burns, Scalds or Bad Legs on the Human Frame.

C.C. undertakes to cure the Epileptic Fits on the Human Frame.

C.C. well understands every disease affecting the Dog and hopes by unremitting attention to the cases entrusted to his care, to obtain a share of public patronage. He can also cure Dogs of any kind of fits.

C.C. undertakes to cure the Mange in Horse, Dogs and Sheep.

C.C. has lived with Lord Gifford as Kennel-man and Kennel-huntsman for several years.

NOTICES

BURROUGHS WELLCOME & Co. announce the introduction of "Wellcome" brand Improved Blackleg Vaccine. Prepared by new methods, the manufacturers inform us, this aluminium hydroxide-absorbed vaccine stimulates a better and more durable immunity in the injected animal in doses less than half those required with the other preparation. Issued in containers of 10 c.c., 20 c.c. and 50 c.c., the dose is 2.0 c.c. for cattle and 1.0 c.c. for sheep.

GLAXO LABORATORIES announce that a veterinary pack of Dimycin solution, 10 grams in 30 c.c., is now available. This preparation provides a combination of streptomycin and dihydrostreptomycin in a handy and economical pack, particularly for large animal practice. Veterinary Vitamin B_1, 10 c.c., is now discontinued.

LEDERLE LABORATORIES LTD. announce that Mr. J. H. Taylor, M.R.C.V.S., has been appointed as their veterinary adviser. He is a graduate of the Royal Veterinary College and was formerly engaged in trials work with the Agricultural Research Council at Compton. He is 26.

ERRATUM

On page 180 of our April issue in the second paragraph we stated trials in Ohio were conducted with "irradiated dried yeast of irradiated ergosterol." This, of course, should read "irradiated dried yeast or irradiated ergosterol."